A STUDY OF VISUAL EVOKED POTENTIALS ,SERUM CALCIUM, FERRITIN AND LIPIDS IN HYPOTHYROID INDIVIDUALS

Dissertation submitted to

THE TAMILNADU DR . M.G.R. MEDICAL UNIVERSITY,

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M.D. (PHYSIOLOGY)

MAY – 2018

DEPARTMENT OF PHYSIOLOGY

TIRUNELVELI MEDICAL COLLEGE

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CERTIFICATE

This is to certify that the dissertation entitled, **" A STUDY OF VISUAL EVOKED POTENTIALS , SERUM CALCIUM , FERRITIN AND LIPIDS IN HYPOTHYROID INDIVIDUALS "** by **Dr. S . ALEEMA BANU** postgraduate in PHYSIOLOGY (2015-2018) , is a bonafide research work carried out under our direct supervision and guidance and is submitted to The Tamilnadu Dr. M.G.R. Medical University, Chennai, for M.D., Degree Examination in Physiology (Branch V), to be held in May 2018.

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This is to certify that the dissertation entitled, **"A STUDY OF VISUAL EVOKED POTENTIALS , SERUM CALCIUM , FERRITIN AND LIPIDS IN HYPOTHYROID INDIVIDUALS "** is a bonafide research work carried out by Dr.S.ALEEMA BANU, post graduate in the Department of Physiology, Tirunelveli Medical College & Hospital , Tirunelveli – 11 under my direct guidance and supervision in partial fulfillment of the requirement for the award of the degree of MD in PHYSIOLOGY (Branch – V) in May 2018.

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DECLARATION

I solemnly declare that the dissertation entitled **"A STUDY OF VISUAL EVOKED POTENTIALS , SERUM CALCIUM , FERRITIN AND LIPIDS IN HYPOTHYROID INDIVIDUALS ''** is done by myself at Tirunelveli Medical College Hospital , Tirunelveli.

The dissertation is submitted to The Tamilnadu Dr. M.G.R. Medical University towards the partial fulfillment of the requirement for the award of M.D. Degree (Branch V) in Physiology.

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PROTOCOL TITLE: A STUDY OF VISUAL EVOKED POTENTIAL, SERUM CALCIUM, FERRITIN & LIPIDS IN HYPOTHYROID INDIVIDUALS.

PRINCIPAL INVESTIGATOR: DR.S.ALEEMA BANU, MBBS.,

DESIGNATION OF PRINCIPAL INVESTIGATOR POST GRADUATE I YEAR IN PHYSIOLOGY
DEPARTMENT & INSTITUTION: TIRUNELVELI MEDICAL COLLEGE , TIRUNELVELI

Dear ,Dr.S.Aleema Banu., MBBS., The Tirunelveli Medical College Institutional Ethics Committee (TIREC) reviewed and discussed your application during the IEC meeting held on 10.12.15.

THE FOLLOWING DOCUMENTS WERE REVIEWED AND APPROVED

1. TIREC Application Form ☐
2. Study Protocol ☐
3. Department Research Committee Approval ☐
4. Patient Information Document and Consent Form in English and Vernacular Language ☐
5. Investigator's Brochure ☐
6. Proposed Methods for Patient Accrual Proposed ☐
7. Curriculum Vitae of the Principal Investigator ☐
8. Insurance /Compensation Policy ☐
9. Investigator's Agreement with Sponsor ☐
10. Investigator's Undertaking ☐
11. DCGI/DGFT approval ☐
12. Clinical Trial Agreement (CTA) ☐
13. Memorandum of Understanding (MOU)/Material Transfer Agreement (MTA) ☐
14. Clinical Trials Registry-India (CTRI) Registration ☐

THE PROTOCOL IS APPROVED IN ITS PRESENTED FORM ON THE FOLLOWING CONDITIONS

1. The approval is valid for a period of 2 year/s or duration of project whichever is later
2. The date of commencement of study should be informed
3. A written request should be submitted 3weeks before for renewal / extension of the validity
4. An annual status report should be submitted.
5. The TIREC will monitor the study
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8. In the events of any protocol amendments, TIREC must be informed and the amendments should be highlighted in clear terms as follows:
   a. The exact alteration/amendment should be specified and indicated where the amendment occurred in the original project. (Page no. Clause no. etc.)
   b. The PI must comment how proposed amendment will affect the ongoing trial. Alteration in the budgetary status, staff requirement should be clearly indicated and the revised budget form should be submitted.
   c. If the amendments require a change in the consent form, the copy of revised Consent Form should be submitted to Ethics Committee for approval. If the amendment demands a re-look at the toxicity or side effects to patients, the same should be documented.
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PLAGIARISM CERTIFICATE

This is to certify that this dissertation work titled **A study of visual evoked potentials , serum calcium , ferritin and lipids in hypothyroid individuals** of the candidate **Dr . S. ALEEMA BANU** with registration Number **201515301** for the award of **M.D. Degree (Branch V)** in the branch of **PHYSIOLOGY** . I personally verified the urkund.com website for the purpose of plagiarism Check. I found that the uploaded thesis file contains from introduction to conclusion pages and result shows **3%** percentage of plagiarism in the dissertation.

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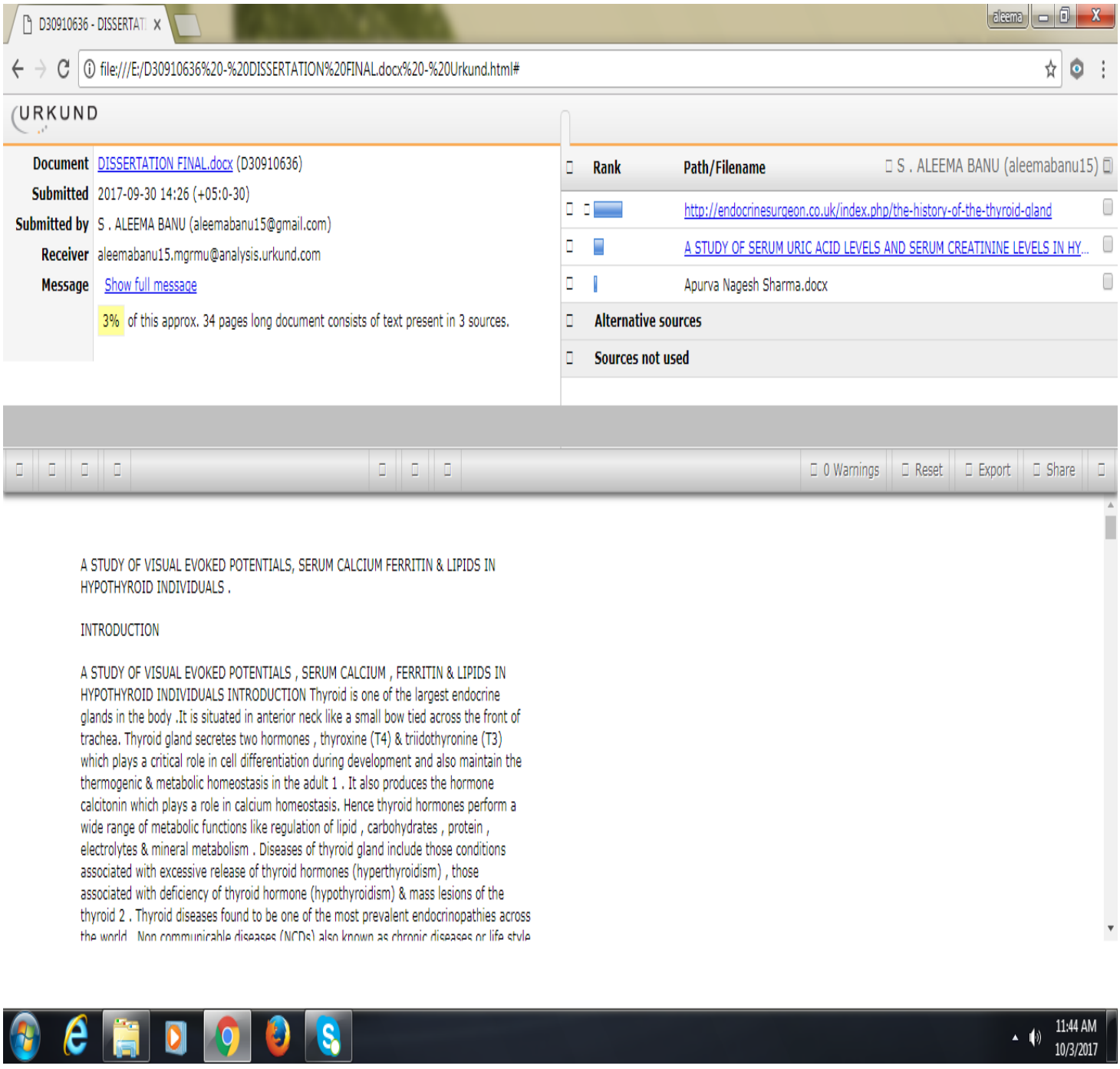

A STUDY OF VISUAL EVOKED POTENTIALS, SERUM CALCIUM FERRITIN & LIPIDS IN HYPOTHYROID INDIVIDUALS .

INTRODUCTION

A STUDY OF VISUAL EVOKED POTENTIALS , SERUM CALCIUM , FERRITIN & LIPIDS IN HYPOTHYROID INDIVIDUALS INTRODUCTION Thyroid is one of the largest endocrine glands in the body .It is situated in anterior neck like a small bow tied across the front of trachea. Thyroid gland secretes two hormones , thyroxine (T4) & triidothyronine (T3) which plays a critical role in cell differentiation during development and also maintain the thermogenic & metabolic homeostasis in the adult 1 . It also produces the hormone calcitonin which plays a role in calcium homeostasis. Hence thyroid hormones perform a wide range of metabolic functions like regulation of lipid , carbohydrates , protein , electrolytes & mineral metabolism . Diseases of thyroid gland include those conditions associated with excessive release of thyroid hormones (hyperthyroidism) , those associated with deficiency of thyroid hormone (hypothyroidism) & mass lesions of the thyroid 2 . Thyroid diseases found to be one of the most prevalent endocrinopathies across the world . Non communicable diseases (NCDs) also known as chronic diseases or life style

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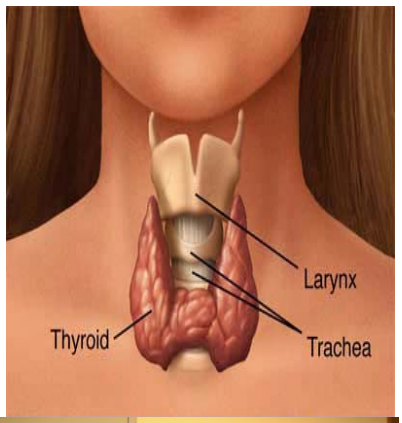
CONTENTS

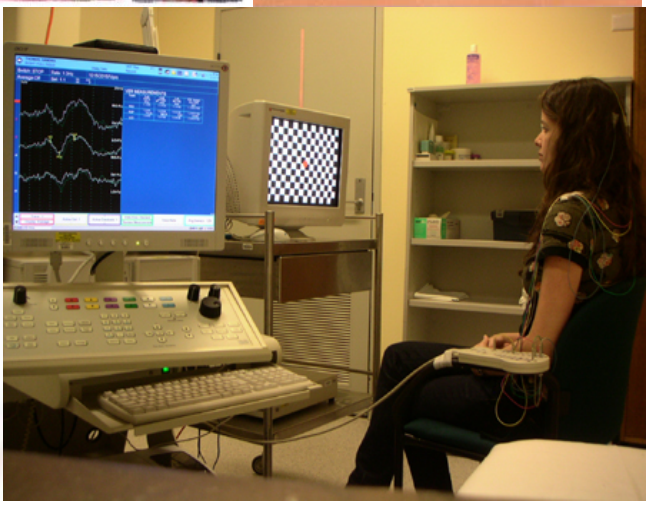
LIST OF ABBREVIATIONS

T_3	Triiodothyronine
T_4	Thyroxine
TSH	Thyroid Stimulating Hormone
NCD	Non Communicable Disease
WHO	World Health Organisation
VEP	Visual Evoked Potential
CNS	Central Nervous System
PNS	Peripheral Nervous System
RMR	Resting Metabolic Rate
BMI	Body Mass Index
NIS	Sodium Iodide Symporter
TPO	Thyroid Peroxidase
TBG	Thyroid Binding Globulin
TRH	Thyrotropin Releasing Hormone
PRVEP	Pattern Reversal Visual Evoked Potential
EEG	Electroencephalogram
PTH	Parathyroid Hormone
CAD	Coronary Artery Disease
LDL	Low Density Lipoprorein

HDL -C	High Density Lipoprotein Cholesterol
HMGCR	3-Hydroxy -3Methyl-Glutaryl Coenzyme A Reductase
SREBP-2	Sterol Regulatory Element Protein – 2
LDL-R	Low Density Lipoprotein cholesterol Receptor
ABC-T	ATP Binding Cassette Transporter
CYP7A1	Cholesterol 7 Hydroxylase
LPL	Lipoprotein Lipase
CETP	Cholesteryl Esters Transfer Protein
LCAT	Lecithin – Cholesterol Acyltransferase
TG	Triglycerides
NCEP - ATP III	National Cholesterol Education Program's Adult Treatment Panel
NHANESIII	National Health and Nutrition Examination Survey
IRE-BP	Iron Regulatory element Binding Protein
IRF	Iron responsive factor
5´-UTR	5´- untranslated region
3´-UTR	3´- untranslated region
VLDL	Very Low Density Lipoproteins

A STUDY OF VISUAL EVOKED POTENTIALS , SERUM CALCIUM, FERRITIN AND LIPIDS IN HYPOTHYROID INDIVIDUALS





INTRODUCTION

STUDY OF VISUAL EVOKED POTENTIALS , SERUM CALCIUM , FERRITIN & LIPIDS IN HYPOTHYROID INDIVIDUALS

INTRODUCTION

Thyroid is one of the largest endocrine glands in the body. It is situated in anterior neck like a small bow tied across and in the front of trachea. Thyroid gland secretes two hormones, thyroxine (T4) & triidothyronine (T3) which plays a critical role in cell differentiation during development and also maintain the thermogenic & metabolic homeostasis in the adult [1] . It also produces the hormone calcitonin which plays a role in calcium homeostasis. Hence thyroid hormones perform a wide range of metabolic functions like regulation of lipid , carbohydrates , protein , electrolytes & mineral metabolism .

Diseases of thyroid gland include those conditions associated with excessive release of thyroid hormones (hyperthyroidism) , those associated with deficiency of thyroid hormone (hypothyroidism) & mass lesions of the thyroid [2] . Thyroid diseases found to be one of the most prevalent endocrinopathies across the world . Non communicable diseases (NCDs) also known as chronic diseases or life style diseases which are not transmissible from person to person & have long duration since they progress slowly. It is a preventable illness , yet it kills 36 million people a year, and it has been

expected to rise to 17-24 % within next decade.The World health Organisation (WHO) defines non communicable diseases (NCD) as a group of conditions which include cancer, diabetes mellitus , cardiovascular diseases, mental health problems, chronic respiratory disease & musculoskeletal conditions & also reports NCDs were the leading cause of mortality in the world [3] . Recently Thyroid Research and Practice highlighted the lack of attention paid to thyroid disorders & emphasized inclusion of thyroid disorders in the list of non communicable disease (NCD) of public health importance [4].

One of the most common forms of thyroid disorder is hypothyroidism. It is caused by any structural or functional derangement interfering with the production of adequate levels of thyroid hormone . So it may be congenital or acquired , primary or secondary , chronic or transient. Iodine deficiency is the most common cause of hypothyroidism worldwide, whereas in iodine sufficiency areas autoimmune disease (Hashimoto's thyroiditis) and iatrogenic causes (treatment of hyperthyroidism) found to more common. The mean annual incidence of spontaneous hypothyroidism during the 20-year follow up of the Whickham cohort was 3.5 per 1000 and 0.6 per 1000 in surving women and men respectively [5].

As per the national workshop held on June 5, 2014 at Chennai , India delegates presented that there were 42 million people in India with thyroid disorders .Hypothyroidism being the commonest thyroid disorders , affecting one in ten adults in India. Its prevalence in India is 11 % comparing with U.K (2%) & USA (4.6%) [6]. According to various studies in hypothyroidism across the world , current prevalence varies from 1% - 20%. In this post iodinization era , a recent epidemiological study conducted in eight cities of India , covering a population of 5376 which highlighted the overall prevalence of hypothyroidism is 10.98% with predominance in females (15.86%) when compared to males (5.02%) & a high titre in older adults when compared with younger individuals[7].

In a study done in 971 adult subjects in Cochin , prevalence of hypothyroidism was 3.9% & subclinical hypothyroidism found to be 9.4%. In another study in India to detect Hashimoto's thyroiditis , 6283 school girls screened all over the country . About 1810 school girls found to have goiter & 764 of them undergone fine needle aspiration cytology & of these 58 (7.5%) had juvenile autoimmune thyroiditis[8]. In some large cohort study, it was found that there is higher prevalence of thyroid dysfunction seen in diabetic individuals. If hypothyroidism remain

undiagnosed it may lead to cardiovascular disease by aggravating dyslipidemia, insulin resistance, obesity, & vascular endothelial abnormalities.

The American Thyroid Association (ATA) recommended that adults must be screened for thyroid function by measurement of the serum thyrotropin concentration at the age of 35 years thereafter for every 5 years [9] . In India , there are about 200 million people at risk of iodine deficiency disorders , even though the most common cause of hypothyroidism is primary failure of thyroid gland . Thyroid function test panel has been widely employed for screening & evaluating thyroid dysfunctions . Biochemically reduction in T3 & T4 concentrations lead to hypersecretion of pituitary TSH leading to elevation of serum thyroid stimulating hormone level (TSH) which is a key laboratory finding for early detection of thyroid failure. Thyroid hormone (T3) has a central role in differentiation , development and maintainence of body homeostasis.

In evaluating the visual system , the sensitivity of psychophysical tests like visual acuity, perimetry & colorvision are unparalleled particularly in a cooperative patient having clear view of fundus. Electrophysiological testing may be necessary when the fundus examination is not possible or there is question of localization of deficit in visual pathway or the patient is malingering/ uncooperative . It is a simple , non invasive & sensitive

technique . Visual evoked potentials (VEP) refers to the electrical potential differences recorded from vertex in response to visual stimuli. It give information of mass response of cotical & subcortical areas. If the entire visual system is intact , a normal cortical response is obtained. Disturbances anywhere in the visual system leads to abnormal VEP.

Pattern reversal VEP (PRVEP) is a useful clinical tool for diagnosing and documenting the visual impairment in pediatric and adult neurological disorders. The rate of pattern - reversal represents the number of times that the pattern changes within a second. Checker board pattern reversal is the most frequently used stimulus in clinical investigations of visual pathway which is presented for 250 ms in the 8 quardrants.Central and peripheral parts of each of the 4 quadrant fields were evaluated. It is found to be more sensitive to the presence of conduction defects in visual pathway .

Thyroid hormone affects both peripheral & central nervous system via its action on gene expression, production of myelin, its effect on neurotransmitter system and axonal transportation . Hence there will be a definite neurological deficit in thyroid deficiency, which involve central nervous system (CNS) more than that of peripheral nervous system (PNS) & at much earlier stage & also increases with increased duration of the

disease.So electrophysiological studies help in early diagnosis of asymptomatic polyneuropathy in hypothyroid individuals.

Calcium, an essential dietary element and humans contain a vast store of calcium (i.e., >1Kg) in their bones . It is an intracellular signaling molecule , which plays a variety of extracellular functions . Calcium plays a key role in many physiological processes which includes contraction of cardiac, skeletal & smooth muscles , blood clotting , transmission of nerve impulses . The components of calcium homeostasis include cell types (eg.neurons) which sense changes in extracellular calcium & release calcium regulating hormones & the target of these hormones , include the kidneys , bones & intestine that respond with changes in calcium mobilization , excretion or uptake. Thyroxine & Calcitonin play a role in calcium homeostasis. Hypothyroidism results in depressed turn over due to impaired mobilization of calcium into the bone which leads to hypocalcemia .

Minerals & trace elements such as iron ,zinc, iodine & selenium found to be essential for normal thyroid hormone metabolism .Iron deficiency anemia results from alterations in resting metabolic rate (RMR). Thyroid hormone is essential for haemoglobin synthesis in adults and maturation of haemoglobin in fetus . Reduced iron or more specifically saying reduced ferritin level found to be one of the most over-looked causes

of low thyroid function [10] . Ferritin , an iron storage protein seen in almost all body tissues & its change in serum concentrations reflect thyroid function. Hypothyroidism is associated with reduced erythrocyte mass due to reduction in plasma volume and hence it is undetectable by routine haemoglobin estimation.

Thyroid hormone enhances fat metabolism by mobilizing lipids rapidly from fat tissues decreases fat stores of the body to a greater extent than almost any other tissue . This in turn increases the free fatty acids in plasma & accelerates its oxidation too. Normally thyroid hormone decreases plasma cholesterol by increasing rate of cholesterol secretion in bile & consequent loss in the feces . So in hypothyroidism , the plasma concentrations of triglycerides, cholesterol, phospholipids are greatly increased which leads to excessive fat deposition in liver. If hypothyroidism remain untreated ,it will lead to increase circulatory plasma cholesterol which results in severe atherosclerosis .

Obesity , a major health concern in developed countries during the last few decades has its own impact not only in adults but also in children. It is an important risk factor for various diseases like metabolic syndrome , diabetes mellitus type 2 & cardiovascular diseases which occurs as a result of complex interactions between a person's genes & environment

characterized by long term energy balance due to excessive calorie intake & reduced energy output[11]. Recent studies evaluated the issue of hormonal changes associated with obesity & demonstrated that the elevation of serum TSH , suggesting subclinical hypothyroidism frequently associated with human obesity .Since obesity has a strong endocrinological & neurological basis and many molecular mechanism involved in its development.[12] .Obesity index or Body mass index done estimates overall fat distribution . Thyroid hormone stimulates changes in physical activity which in turn to the body mass and TSH levels usually correlate with body weight [13].

There are only very few studies relating hypothyroidism with visual evoked potentials , serum ferritin , serum calcium and lipid profile . All these investigations even though bit costlier is freely available in our Government hospitals . But many hypothyroids, still wandering undiagnosed due to lack of awareness . So in our study , we decided to investigate these parameters in those subjects at the earliest and to prevent the hypothyroids from progressing to serious neurological and cardiovascular complications.

AIM

&

OBJECTIVES

AIM AND OBJECTIVES

AIM

- To study about the visual evoked potentials , body mass index, serum calcium , serum ferritin and lipid profile in hypothyroids and compared with the controls.

OBJECTIVES

- To find the correlation between serum Calcium and TSH.
- To find the correlation between serum Ferritin and TSH.
- To determine the association of obesity index / (BMI) with TSH.
- To determine the association between lipids and thyroid hormones in hypothyroidism.

REVIEW
OF LITERATURE

THE HISTORY OF THE THYROID GLAND

In 1600 BC , the Chinese used burnt sponge and sea weed for the treatment of goiters . Celsus first described a bronchoceole (tumour of the neck) in 15 AD. Around this period Pliny referred to epidemics of the goiter in the Alps & recommended the use of burnt sea weed for treatment. In 150 AD , Galen referred "spongia usta" for the treatment of the goiter. In 650 AD , Sun Ssu – Mo used a combination of seaweed , dried powdered mollusc shells and chopped up thyroid gland for the treatment of goiters . In 990 AD , Ali-ibn- Abbas was the first to discuss surgery for treating goiter. Some fifty years later , Paracelsus attributed goiters to mineral impurities in water. Finally in 1656, Thomas Wharton named it the thyroid gland , meaning shield due to its shape , as it resembled the shields used by Ancient Greece.

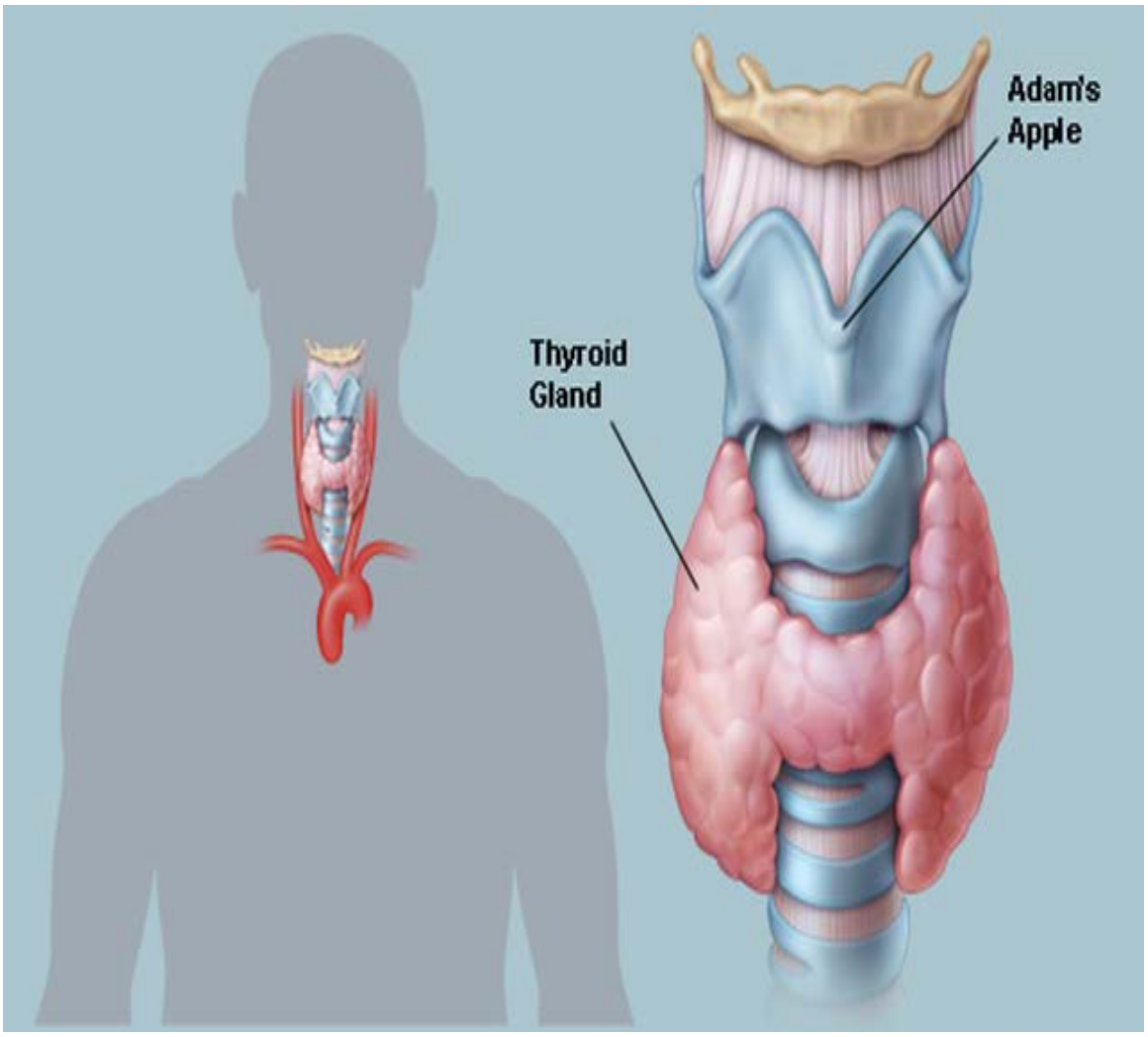
In 1811 , Paris discovered iodine in the burnt ashes of sea weed & the idea that it was the active ingredient in the treatments that were prescribed for goiters was developed . Ten years later Prout was the first to recommend iodine in treating goiter . On the European Continent , exophthalmic goiter is known as Basedow's disease . Karl Adolph Basedow had described the entity independently in 1840. Sir William Gull ,physician to Queen Victoria, although not the first to recognize the condition of

myxoedema (hypothyroidism) , was the first to attribute it to atrophy of the thyroid gland.

In 1880, Theodor Kocher demonstrated that total thyroidectomy caused hypothyroidism but initially thought that the symptoms were due to chronic airway obstruction . Kocher won the Nobel prize in Physiology or Medicine in 1909 “for his work on pathology , physiology & surgery of the thyroid gland ”[14]. The idea that thyroid produces an iodine containing substance was investigated in the last century. In 1914, Edward Calvin Kendall isolated thyroxine ,which is an active hormone of the thyroid gland.

In 1912, Hakaru Hashimoto documented a case of Hashimoto’s thyroiditis & autoantibodies were demonstrated in 1956 [15] . Many authors described cretinism, myxoedema their relationship with thyroid in nineteenth century. Modern treatments and investigative modalities evolving through out the mid twentieth century , including the use of radioactive iodine , thiouracil and fine needle aspiration biopsy.[16]

THE THYROID GLAND



PHYLOGENY

In the phylogeny of thyroid gland , its embryogenesis and certain functions shows its primitive relation to the gastrointestinal tract . In higher vertebrates , control of TSH secretion is in turn , influenced by a TSH releasing hormone (TRH) of hypothalamic origin [17] (**Gorbman A. et al 1978)** Because of this phylogenetic association , the salivary and gastric glands like the thyroid , are capable of concentrating iodide in their secretions many times over, eventhough iodide transport in these sites is not responsible to stimulation of thyrotropin (TSH). According to **Stanbury et al (1978)** in rare form of goitrous hypothyroidism due to lack of thyroid iodide transport mechanism , the salivary transport of iodide is defective[18].

EMBRYOLOGY OF THYROID

Thyroid tissue is found first in vertebrates , it is a single bilobed gland in front of the trachea . In man , the isthumus connecting two lobes crosses the front of the second and third tracheal rings .Thyroid gland derived from the midline endoderm which can be recognized in the developing embryo at the end of first month . It develops as an outgrowth of the foregut at a point later marked by the foramen caecum of tongue .The course of descent is indicated by the thyroglossal duct which occasionally

persists . The pyramidal lobe , an upward extension of thyroid isthmus , is a residue of the thyroglossal duct[19] .

ANATOMY OF THE THYROID

The thyroid gland, a butterfly shaped gland that straddles trachea in front of the neck .In adults it weighs approximately 20 grams . A small connecting branch or isthmus connects the right and left lobes of thyroid gland . The right lobe of is slightly larger than the left lobe . The thyroid gland possesses many features unique among endocrine glands , not the least of which is that it is the only endocrine gland can be easily seen and palpated in the course of routine clinical examination . A convenient clinical standard in assessing goiter size is that each lobe should not exceed the size of the terminal phalanx of the subject's thumb.

BLOOD SUPPLY

There are four main arteries , the paired superior and inferior thyroid arteries . An inconstant fifth artery thyroidea ima , may occasionally be a large vessel . In addition the tracheal and oesophageal arteries contribute to many unnamed branches which are normally small but which enlarge in thyrotoxicosis and may bleed briskly during thyroidectomy. The veins

draining the thyroid collect into three paired channels , the superior , middle and inferior thyroid veins.

LYMPHATICS

The main lymphatic vessels leave the gland in two groups , ascending and descending . Ascending lymphatics from the isthmus and from the medial part of the lateral lobes , pass upwards to lymph nodes in front of the larynx. Ascending lymphatics from the rest of the lateral lobes pass upwards and backwards to lymph nodes lying along the upper part of the internal jugular vein. Descending lymphatics from the isthmus and medial part of lateral lobes pass down to the pretracheal and retrosternal lymph nodes and descending lymphatics from the rest of the lateral lobes pass laterally to lymph nodes along the lower part of internal jugular vein.

INNERVATION

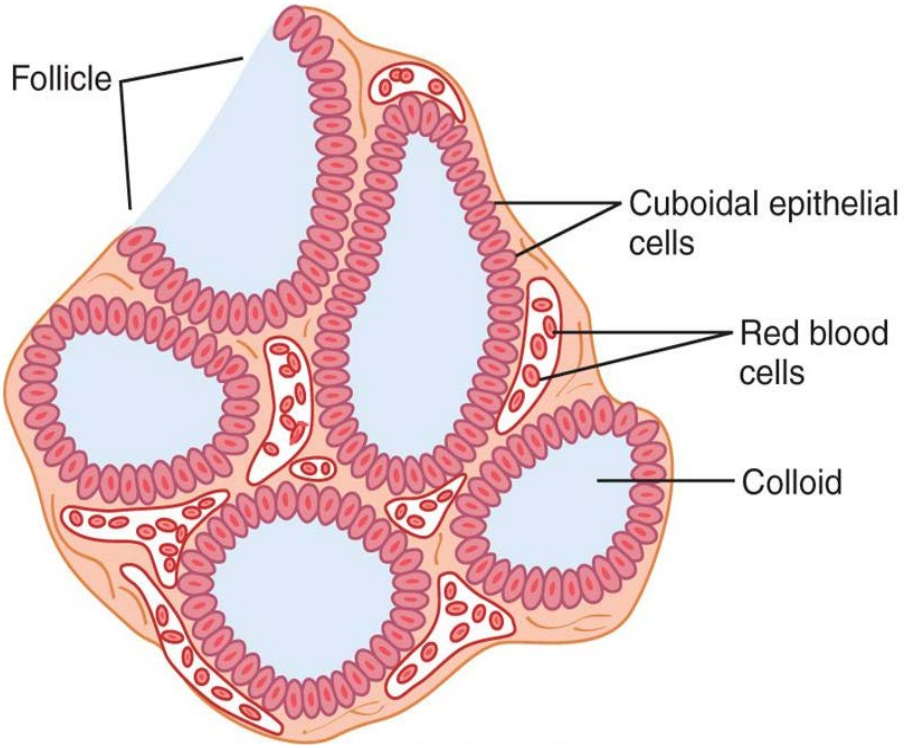
Thyroid receives both sympathetic and parasympathetic nerve fibres . They control the blood flow rather than the secretions . Sympathetic fibres emerge from middle cervical ganglion and pass into the substance of the gland in the peri-arterial plexus of the superior and inferior thyroid arteries . Parasympathetic fibres are derived from the superior and recurrent laryngeal

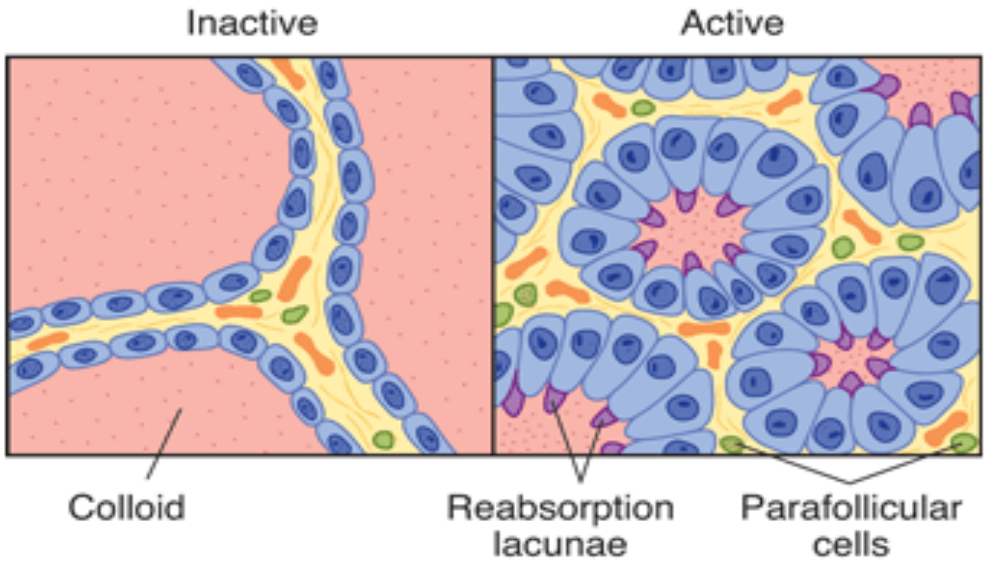
branches of the vagus . Denervation of the thyroid does not alter its histological appearance nor does it alter the basal metabolic rate.

HISTOLOGY OF THYROID GLAND

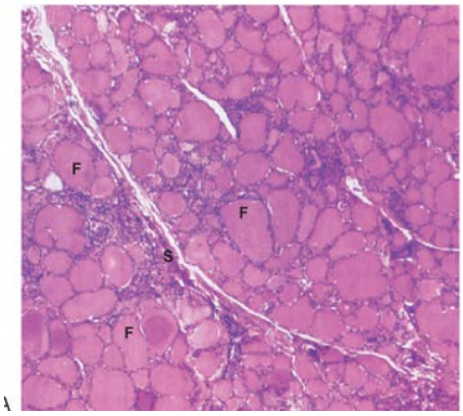
Thyroid follicle is the functional unit of the thyroid gland ,which is a spherical structure about 200 to 300 µm in diameter that is surrounded by a single layer of thyroid epithelial cells . The epithelium sits on the basal lamina , the outermost structure of the follicle surrounded by rich capillary supply .The apical side of the follicular epithelium faces the lumen of the follicle. The lumen is filled with colloid , which is composed of thyroglobulin which is secreted and iodinated by the thyroid epithelial cells. The size of the epithelial cells and amount of colloid are the dynamic features which changes with the activity of the gland. The epithelial cells are flat in the resting state and tall when the gland is active . Scattered within the gland are the parafollicular cells called C cells , being derived from neural crest rather than endoderm .

THE THYROID FOLLICLES

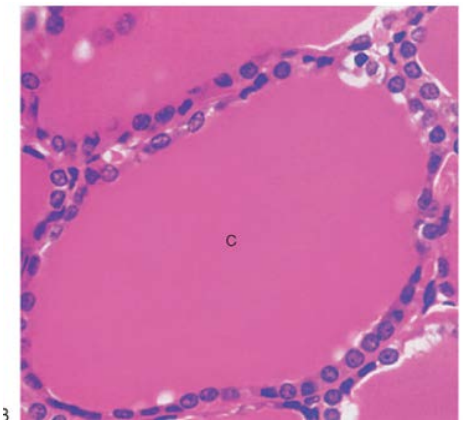




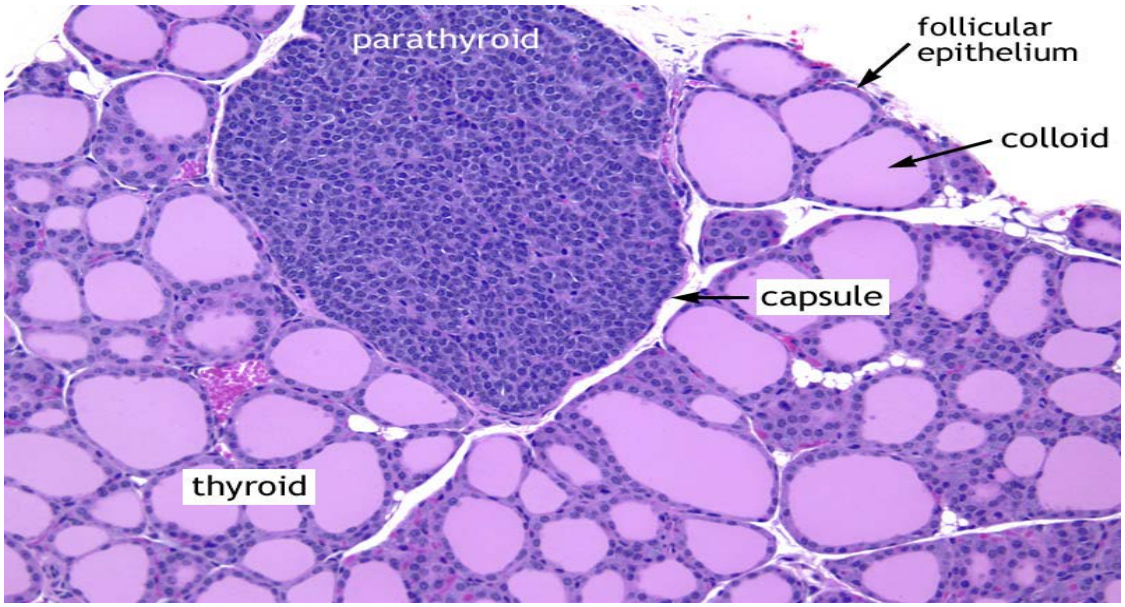
HISTOLOGY OF THYROID FOLLICLES



F - FOLLICLES



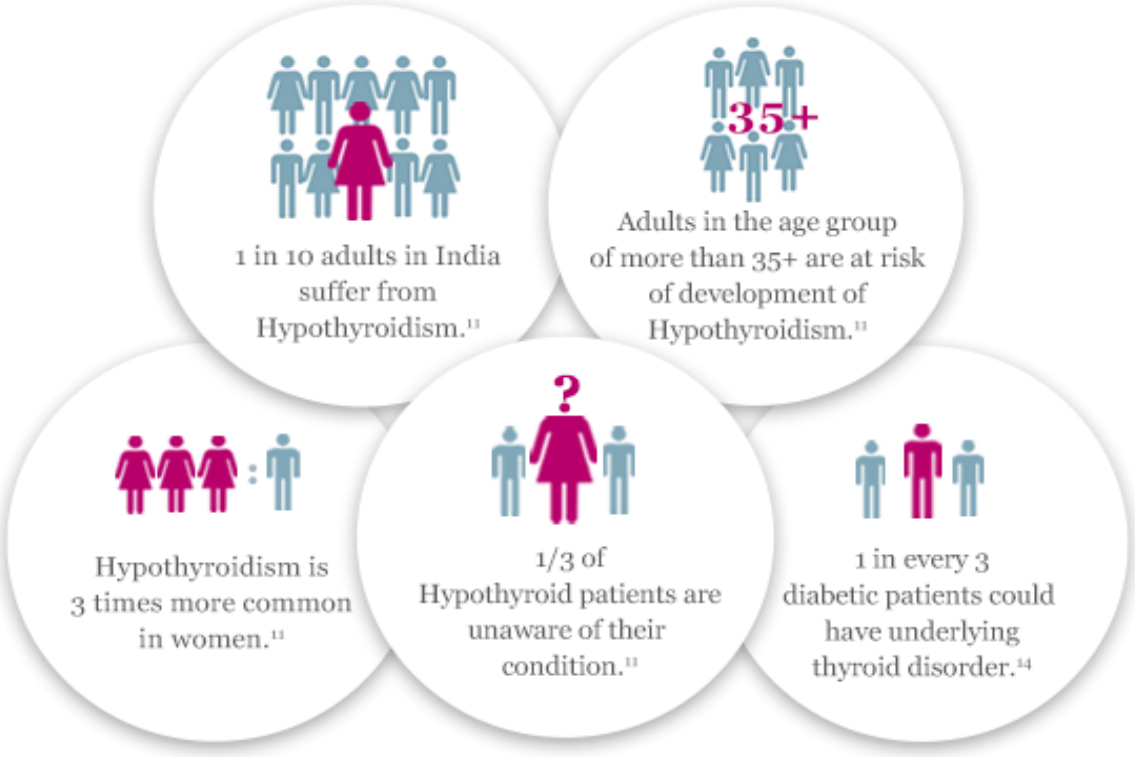
C - COLLOID



EPIDEMIOLOGY OF HYPOTHYROIDISM

An estimated 4.2 crores Indians suffering from thyroid disorders . About 4-10 % of general population may have hypothyroidism . Symptoms of thyroid disorders are commonly confused with those of other diseases, hence majority of patients remain undiagnosed and untreated . Prevalence in developed world is estimated to be about 4-5% . **1 in 10 Indians suffer from thyroid disorder .**

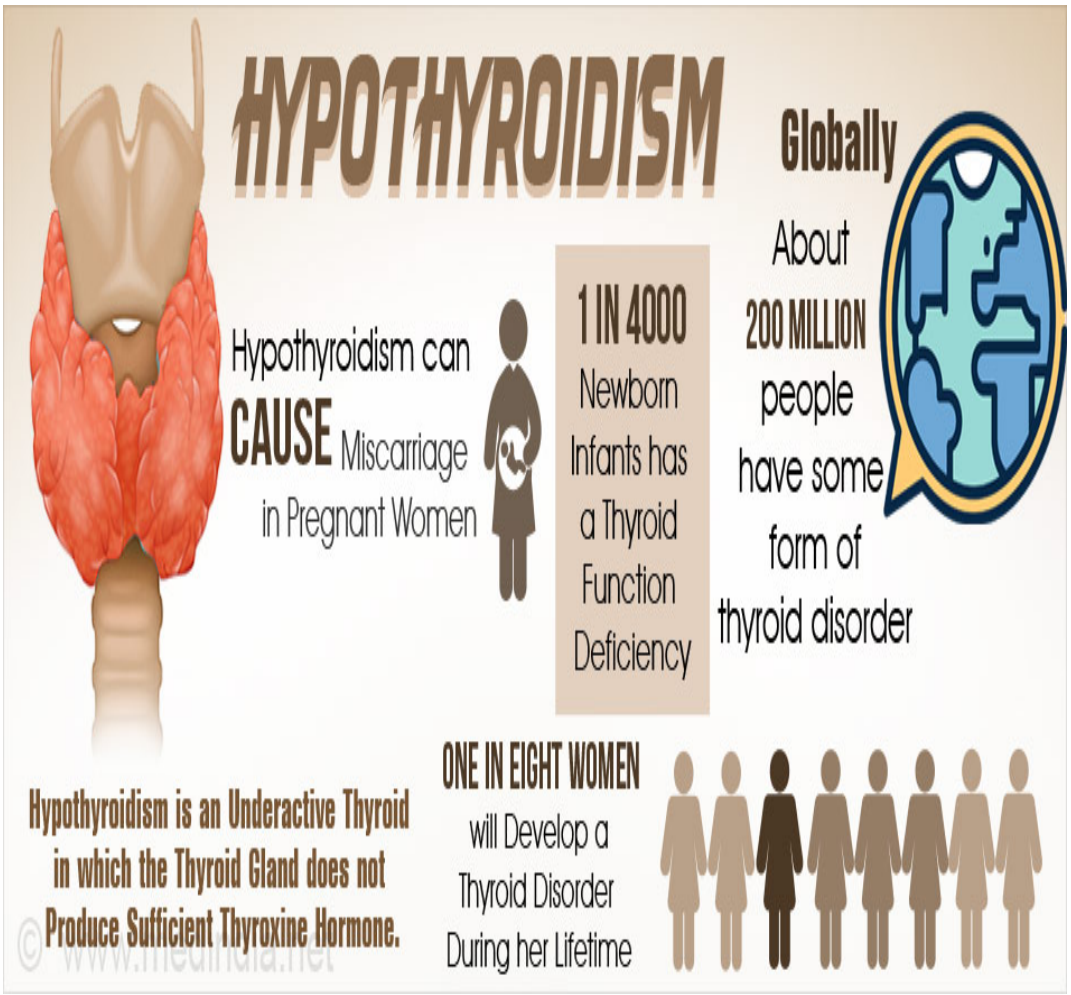
(The Times of India, Aug30, 2017)



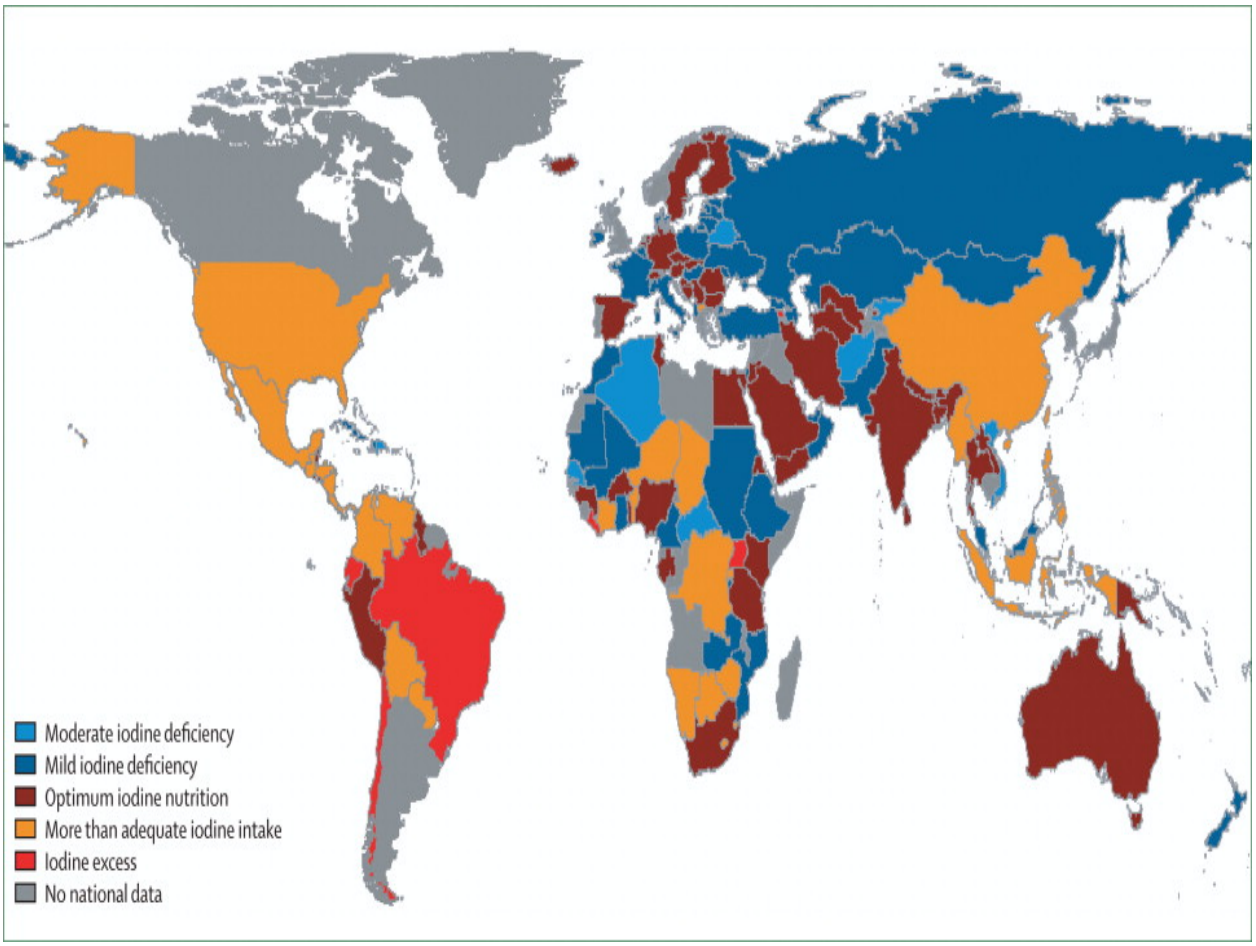
PREVALENCE (MALE : FEMALE)

British Thyroid Association. 2006. UK Guidelines for the Use of Thyroid Function Tests. Available at: http://www.british-thyroid-association.org/info-for-patients/Docs/TFT_guideline_final_version_July_2006.pdf. Last accessed March 2015.

HYPOTHYROIDISM - FEMALE PREPONDERANCE



IODINE DEFICIENCY AREAS



Nearly 2 million individuals worldwide have insufficient iodine intake, particularly in south Asia and sub-saharan Africa are affected .Iodine deficiency has many adverse effects on growth and development .These effects are due to inadequate production of thyroid hormones

World Thyroid Day globally recognized **on May 25th** American thyroid association collaborates with international thyroid societies

The important goal of the ATA and our sister thyroid organizations is to get the word out about Thyroid!

Perhaps the most stunning statistics are that up to 60 percent of those with thyroid disease are unaware of their condition and that women are five to eight times more likely than men to have thyroid problems.

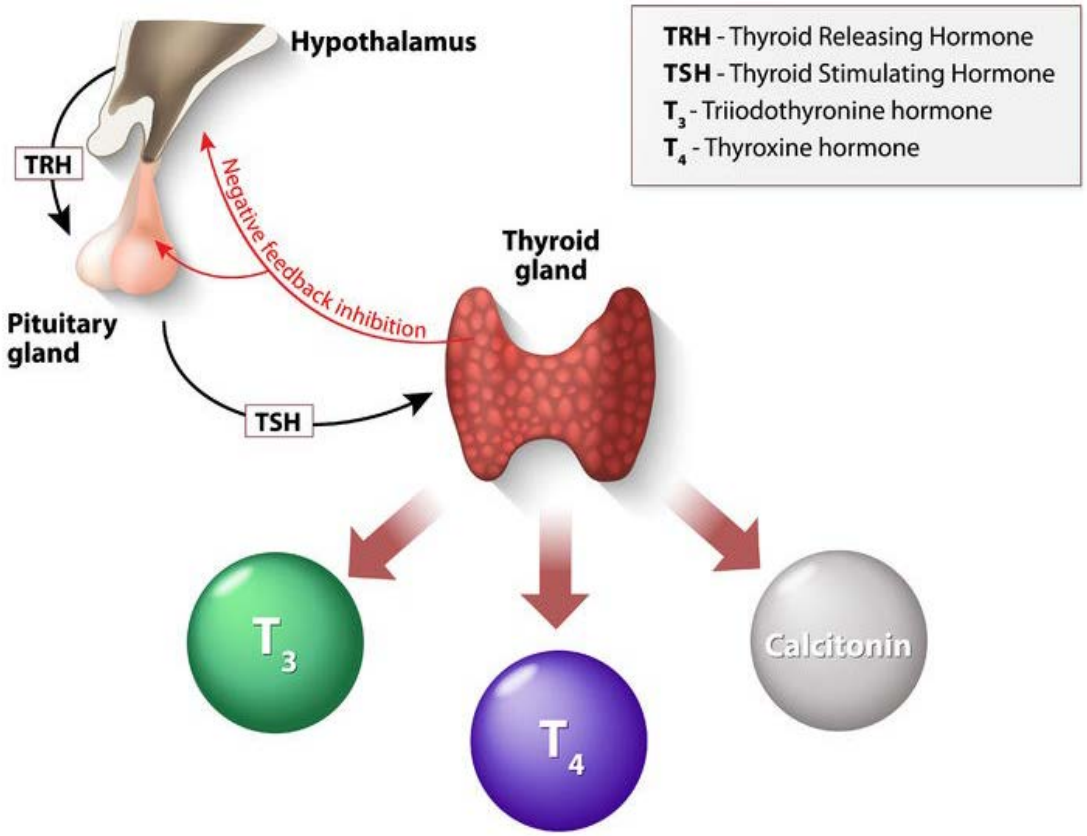
ORGANISATIONS FOR SCREENING THYROID

Recommendations of Six Organizations Regarding Screening of Asymptomatic Adults for Thyroid Dysfunction	
Organization	**Screening recommendations**
American Thyroid Association	Women and men >35 years of age should be screened every 5 years.
American Association of Clinical Endocrinologists	Older patients, especially women, should be screened.
American Academy of Family Physicians	Patients ≥60 years of age should be screened.
American College of Physicians	Women ≥50 years of age with an incidental finding suggestive of symptomatic thyroid disease should be evaluated.
U.S. Preventive Services Task Force	Insufficient evidence for or against screening
Royal College of Physicians of London	Screening of the healthy adult population unjustified

THE THYROID HORMONE

Thyroid hormones are the only ones that require essential trace element iodine , for the production of active hormones . Another unusual feature of thyroid hormone physiology in extracellular site within a highly proteinaceous material called thyroid colloid . The major protein within this material is thyroglobulin , part of its primary structure contains the thyroid hormones thyroxine (tetraiodothyronine or T4)) and triiodothyronine (T_3) . Another unique aspect of thyroid is there is no cell membrane receptors exists for these hormones and they act by binding to nuclear receptors & regulate the transcription of cell proteins. These hormones act on multiple tissues hence they are essential for normal growth, metabolism & development. C cells (parafollicular cells) which are not part of follicular unit play role in calcium & phosphate homeostasis.

THYROID HORMONES



SYNTHESIS OF THYROID HORMONES

- **Iodinating tyrosine residues on thyroglobulin and are stored as part of thyroglobulin molecules in thyroid follicles**

T_4 is less active than the T_3 . Reverse T_3 (rT_3) has no biological activity . They derived from ether linkage of a tyrosine molecule to the benzyl group of a second tyrosine molecule . Each benzyl group is attached to one or two iodine atoms. Thyroid gland start synthesis by trapping of iodide . Iodine which exists in nature as trace element in soil, has been incorporated in many foods , is essential for thyroid hormone formation.The minimum daily iodine requirement to maintain normal functioning of thyroid is 150µg . Supplementation of table salts can provide average dietary intake 500µg/ day approximately . The gastrointestinal tract rapidly absorbs the iodide anion (I^-) which is taken up by thyroid gland actively. The Na/I cotransporter (NIS) , a 65 kDa integral membrane protein located at thyroid follicular cell's basolateral membrane and is said to have twelve membrane spanning protein segments . Low levels of iodine increase the amount of NIS and stimulate uptake whereas high iodine levels suppress NIS expression and uptake. NIS moves I^- into follicular cells against the I^-

electrochemical gradient ,which is fueled by the Na^{+} electrochemical gradient energy **(Iodide trapping)** .The iodide leaves the follicular cell and enters follicular lumen , across the apical membrane **. Pendrin** , which is a member of SLC26 belong to family of anion exchangers located on the apical membrane contribute I^{-} secretion . The thyroid may enlarge due to deficient I^{-} uptake which may result from an I^{-} deficient diet .The follicular cells secrete **thyroglobulin** into the follicular lumen and the thyroglobulin has the tyrosyl groups into which the I^{-} attach ultimately. Thyroglobulin molecule is a very large glycoprotein (> 600kDa) accounting nearly half of the protein content of the thyroid gland . It contains very few tyrosyl residues (~ 100 per molecule of thyroglobulin) and only few of these (< 20) will be subjected to iodination . Also the secretory vesicles containing thyroglobulin carry **the enzyme thyroid peroxidase (TPO)** on their intravesicular surfaces . When these vesicles fuse with the apical membrane , this enzyme will face follicular lumen and hence catalyzes the oxidation of I^{-} to I^{0} . Thyroglobulin enters the follicular lumen by exocytosis and its tyrosyl groups react with I^{0}. Then one or two oxidized atoms will incorporate selectively into the specific tyrosyl residues within the thyroglobulin molecule **(Organification)** . So an internal rearrangement occurs which

result in conjugation of two iodinated tyrosyl residues to form a single iodothyronine and dehydroalanine as remnant . Both of them remain as part of the primary structure of the iodinated thyroglobulin until it is degraded into the follicular cell. Also coupling of two tyrosines , catalysed by TPO will not occur unless they are iodinated .Thyroid hormones are still part of the thyroglobulin molecule , are stored as colloid in thyroid follicle.

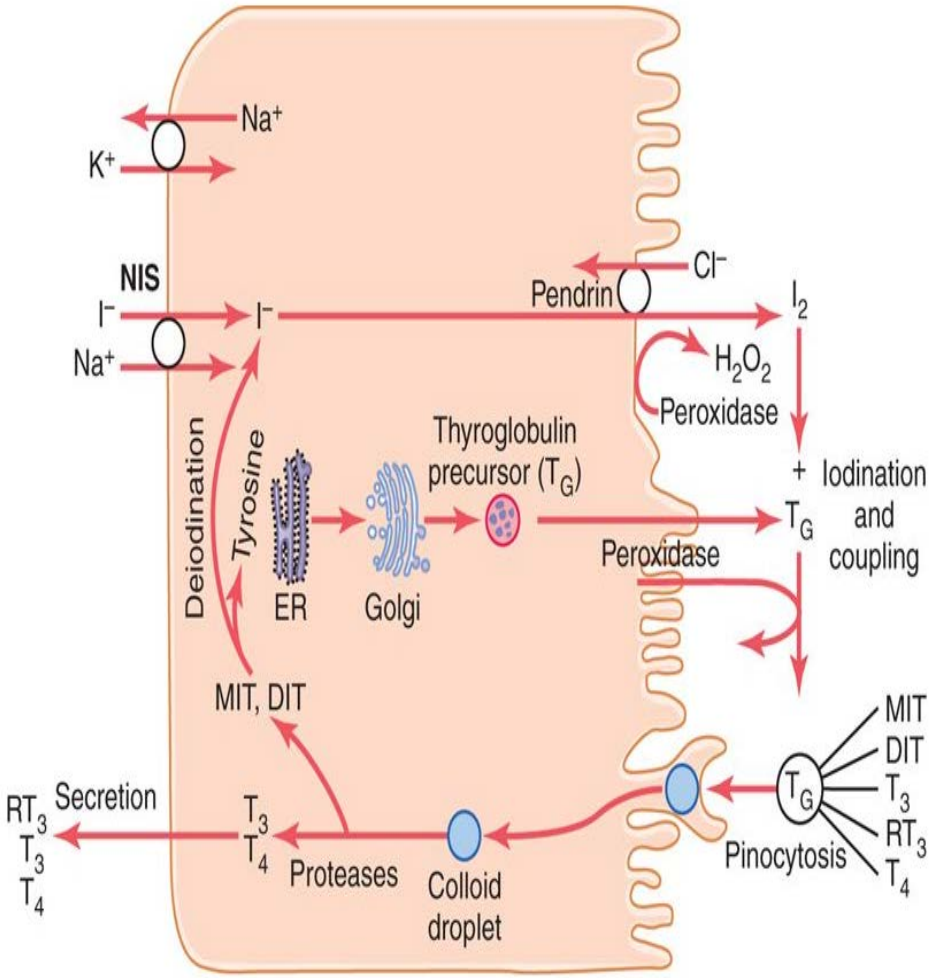
- **Iodinated thyroglobulin taken up by follicular cells which hydrolyzed and release T_4 and T_3 into the blood to bind with thyroid binding globulins and other proteins .**

Thyroid hormones will remain inactive until the iodinated thyroglobulin hydrolysed . Follicular cells must resorb the thyroglobulin from lumen by fluid – phase endocytosis. This endocytic vesicle containing the colloid droplet moves from the apical toward the basolateral membrane, fuses with lysosome forming lysoendosome.Within the vesicles , the thyroglobulin is hydrolyzed forming T_4 and T_3 as well as diiodothyronine and monoiodothyronine **(coupling).** T_4 and T_3 released from the vesicle near basolateral membrane into the circulation . 90% of thyroid hormone secreted will be released as T_4 and 10% will be released as T_3. Non

thyroidal tissues metabolise the T_4 to T_3 and rT_3. Approximately three fourths of circulating T_3 obtained from the peripheral conversion of T_4, usually occurs principally in the liver and kidneys. Both T_4 and T_3 highly bound to plasma proteins in the circulation such as albumin, thyroid binding globulin (TBG) and transthyretin (TTR) which account for most of this binding. Liver makes each of the thyroid binding proteins.

SYNTHESIS OF THYROID HORMONES

Blood **Thyroid Follicular Epithilial Cells** **Lumen**



TBG is a 54 –kDa glycoprotein . The affinity of binding proteins is more for T_4 (> 99.98 %) than T_3 which is slightly less bound (~99.5%) . These free and unbound hormone in the circulation is responsible for the actions of the thyroid hormones on target tissues and the bound hormonal forms can vary substantially with the amount TBG in different physiological states. But the concentration of free forms do not change. The binding to plasma proteins prolongs the half –lives of both T_4 (8days) and T_3 (~ 24 hrs). T_4 in plasma (10:1) provide reserve of prohormone for synthesis of T_3 ,which is responsible for most of the biological activity.

- **Selective Deiodination of T_4 to T_3 by peripheral tissues**

Certain tissues in the body will deiodinate T_4 producing T_3 and rT_3 ,which is further deiodinated to various DITs and MITs .The importance of peripheral deiodination is observed in persons who have removed thyroids yet they have normal concentration of T_3,when supplemented by oral T_4.Two types of deiodinases which convert T_4 to T_3 . It is 5´/3´ - deiodinase which removes the iodine (I) from outer ring , thus forming T_3 and when iodine (I) is removed from inner ring inactive r T_3 will be formed. 5´/3´-deiodinases on outer ring exists in two forms. Type 1 exists in high amounts

in liver, kidney and thyroid and type2 seen in placenta pituitary and central nervous system (CNS).

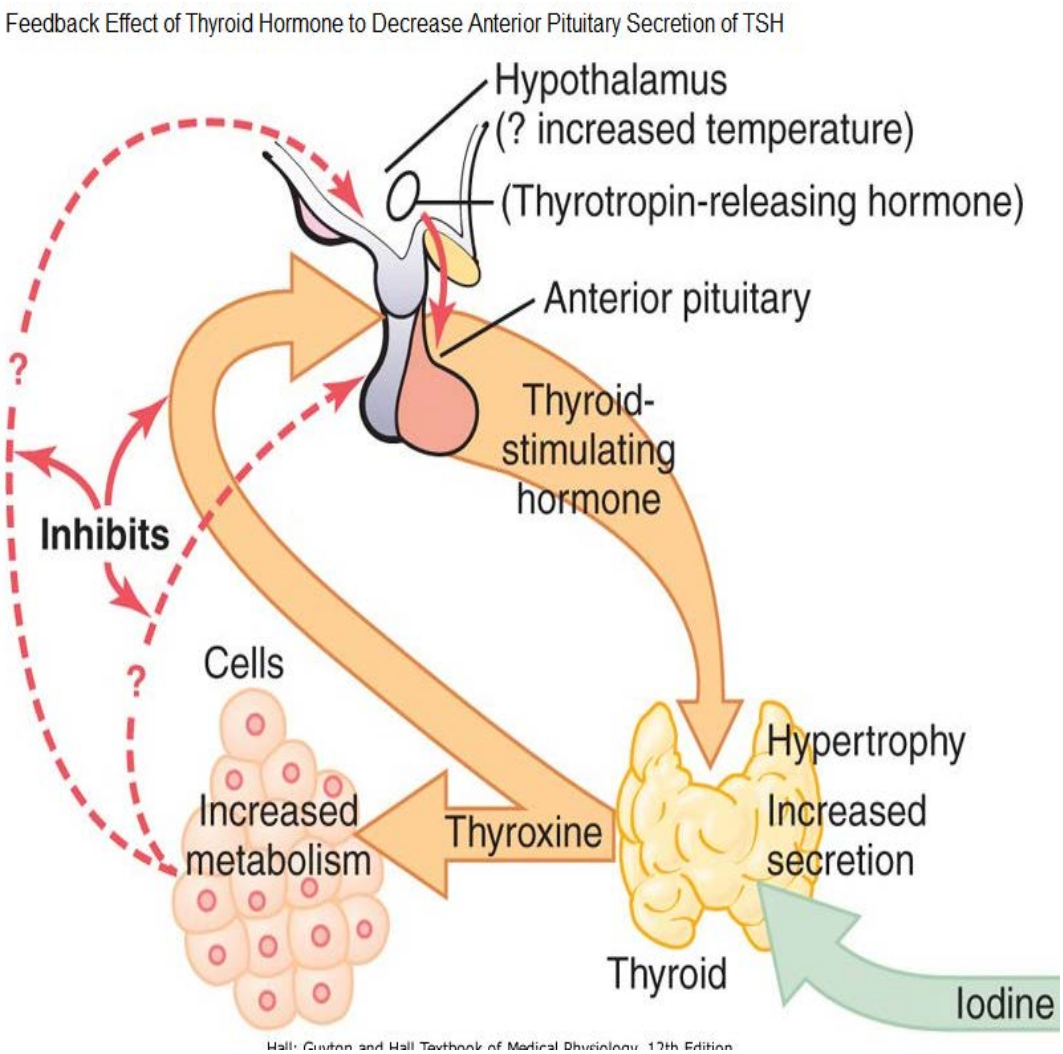
REGULATION OF THYROID HORMONES

Two mechanism involved in the regulation of TSH from anterior pituitary negative feed-back exerted by concentration of circulating thyroid hormones[21]. High levels of free T_4 and T_3 act on anterior pituitary and rapidly reduce TSH secretion and decrease T_4 and T_3 by thyroid .But low levels of thyroid hormones stimulate TSH secretion from pituitary and increase thyroid hormone secretion .

Hypothalamus produces the thyrotropin releasing hormone (TRH) which stimulates TSH secretion from anterior pituitary. Increase in TSH secretion by cold and reduced secretion by warmth is due to the action of hypothalamus.

REGULATION OF THYROID HORMONES -

(Negative Feedback loop)



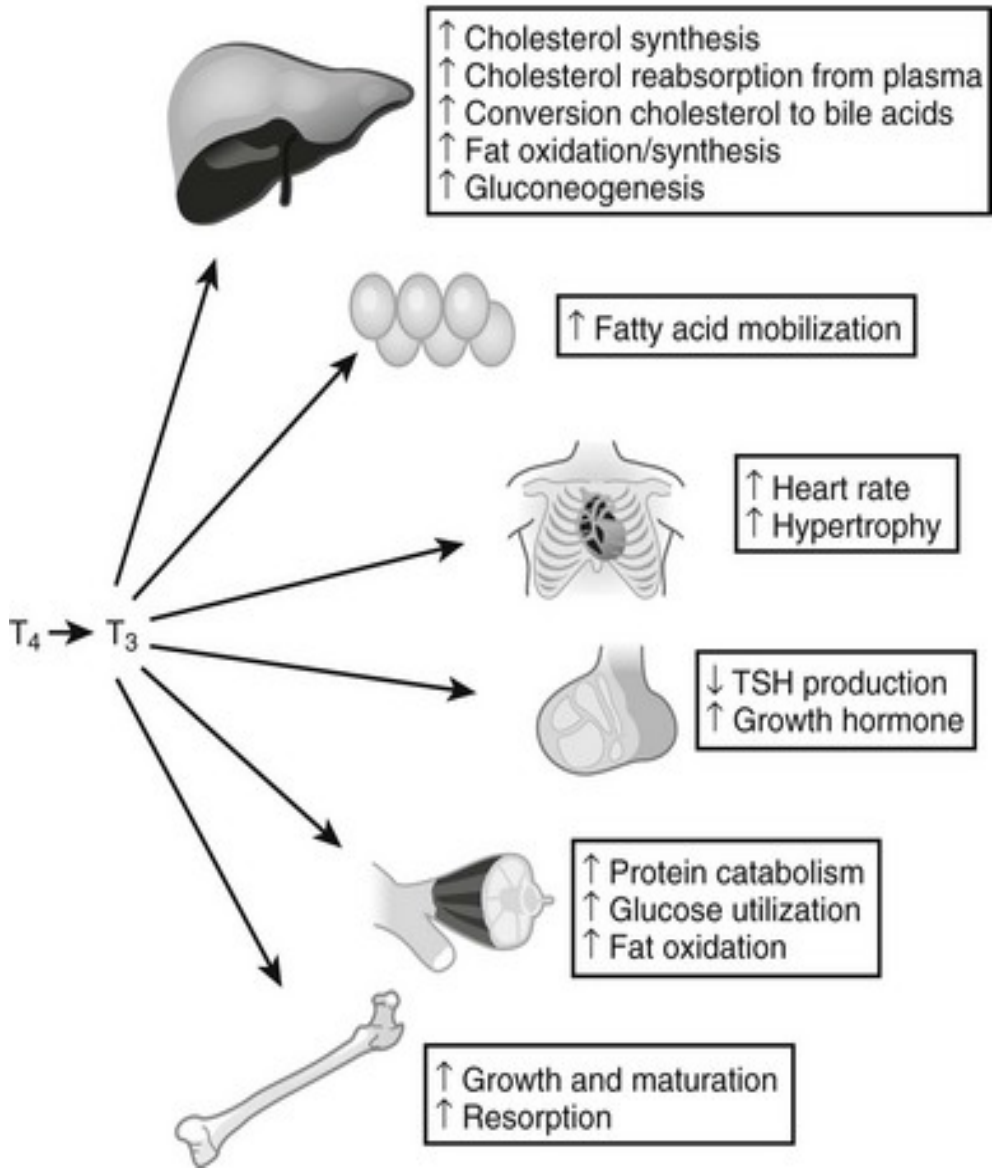
Circulating T_4 and T_3 also exert feed - back effects via hypothalamus. Iodine has got unique role in the function of thyroid. Optimum iodine intake is needed for hormone function. Too little iodide decreases thyroid hormone levels.

ACTION OF THYROID HORMONES

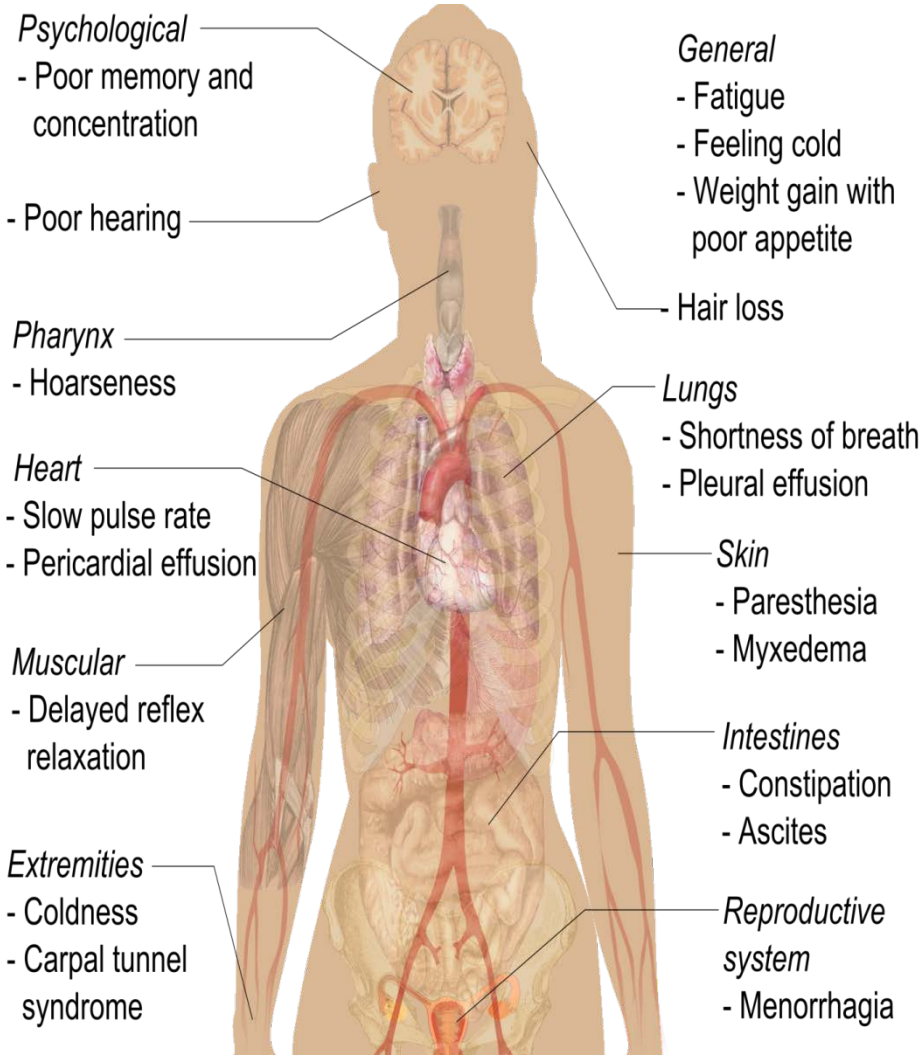
Thyroid hormones is essential for normal proportions of the body , skeletal growth and maturation , normal contours of face , ossification of cartilage, formation and eruption of teeth .Thyroxine has permissive action on growth hormone. Thyroid hormone is necessary for the development of central nervous system and brain growth and it should be present in adequate amount at birth and during the first year . It is also necessary for general metabolism and calorigenesis. They are the regulators of cellular oxidative mechanism and maintain the metabolism of all tissues except brain , lymphnodes , gonads , spleen , accessory sex organs and lung but decreases oxygen (O2) consumption of anterior pituitary. In all other tissues O2 consumption , carbondioxide output (CO2) , heat production and basal metabolic rate are increased. Catecholamines increases the metabolic effects of thyroid hormones. Thyroid hormone increases glucose absorbtion , glycogenolysis , peripheral utilization of glucose Thyroid hormone increases the ability of the liver to excrete cholesterol in bile to a greater extent ,

thus reducing serum cholesterol. Thyroxine promotes protein anabolism and increase protein synthesis and nitrogen retention thereby positive nitrogen balance favouring growth. Excess thyroxine causes dimeralisation of bone. Thyroxine is essential for the conversion of carotene to vitamin A in liver. Thyroid hormones increases cardiac output, heart rate , force of contraction , systolic blood pressure and pulse pressure . It increases the number of β – adrenergic receptors in the heart . It increases the production of myosin with a high ATPase activity in both cardiac and skeletal muscle .Optimal thyroxine is essential for efficient muscle function and for normal gonadal function , Thyroxine stimulates erythropoiesis. Thyroid hormone exerts permissive action on the calorigenic effect of adrenaline. Respiratory rate and depth may be increased due to increased metabolism Gastrointestinal motility , secretion and apetite are also increased .

ACTIONS OF THYROID HORMONES



SYMPTOMS & SIGNS OF HYPOTHYROIDISM



Thyroid stimulating Hormone (TSH)

Thyroid stimulating hormone (TSH) produced by anterior pituitary primarily regulates thyroid function. It is important for normal structural development and secretary activity of thyroid gland .TSH excess causes hyperplasia and increased hormone secretion .TSH combine with cell membrane receptors thereby activate adenylate cyclase which cause increase in cyclic AMP inside the cell. Secretion of TSH is regulated by two mechanisms . Negative feedback mechanism exerted by the concentration of circulating thyroid hormones . High levels of free T_4 and T_3 will act on anterior pituitary and rapidly reduce TSH secretion but low levels of hormones stimulate TSH secretion from pituitary thereby increase thyroid hormone secretion.

Thyrotropin releasing hormone (TRH) produced by hypothalamus stimulate release of TSH .TSH secretion is increased by cold and secretion decreased by warmth is due to hypothalamus .Feed back effects exerted by circulating T_3 and T_4 via hypothalamus do occur in these conditions.

Iodine plays a unique role in thyroid function . Optimum intake of iodine is essential . Too little iodide decrease whereas, too much iodide intake increase thyroid hormone secretion.

Currently according to **American thyroid association (ATA)** guidelines thyrotropin (TSH) , free thyroxine (FT_4) or FT_4 combined with Total triiodothyronine (TT_3) is recommended for use as indicators in laboratory testing to assess thyroid function clinically [22 , 23] . According to **Castellano , Laurin et al (2013)** , TSH is considered as the most important indicator in the evaluation of thyroid function [24] . However the fact that serum FT_4 and FT_3 do not match the clinical manifestations to some extent caused by the interference of measurement methods [25,26] **(S.Ghosh , Collier et al (2008).** From the clinical practice , the measurement of serum FT_4 is an indirect assessed value and is less stable and repeatable compared with TT_4 . **Evenlin Mingote (2012) et al** and other scholars thought that patients with elevated levels of TSH and decreased TT_4 but not FT_4 in hypothyroidism had a worst prognosis [27] . Hence the clinical value of TT_4 may be greater than FT_4 in evaluation of thyroid function in hypothyroidism . So in our study , newly diagnosed hypothyroids were selected under the laboratory criteria of low total T_4 and TSH > 10μIU/ml.

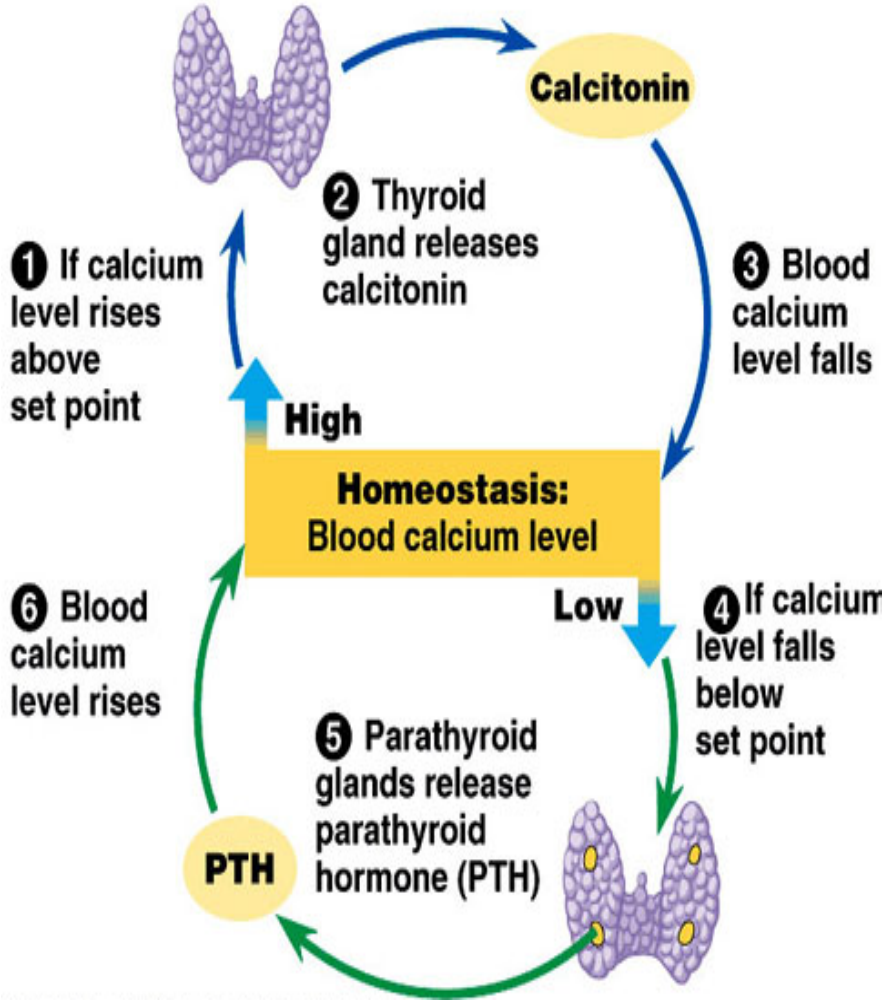
Visual evoked potentials (VEP) is a simple , non invasive, sensitive technique for evaluating impulse conduction along the optical pathway . Full-field PRVEP testing is most sensitive in detecting lesions of the visual system anterior to the optic chiasm. The majority of P100 response arises in

the neural elements of the eye subserving the central 8-10 degrees of the visual field . Records are analysed to identify the major response components like N75, P100, N145 components in the occipital regions and the N100 in the mid frontal region. Of these P100 is the most consistent and least variable peak .The P100 must be positively identified by its topographic distribution ,demonstrating maximal amplitude at the midoccipital site**.** [28,29] . It must be distinguished from other positive polarity peaks that may occur with the disease eg. central scotoma **(Halliday et al (1979) ; Jones and Blume (1985) et al .** If P100 maximal amplitude is displaced to one of the lateral occipital regions then additional testing with hemi-field or partial-field stimulation will be necessary for definite peak identification . According to guide line 9B of VEP of **American Clinical Neurophysiology Society (2008)** states that the most clinically useful measurements on the responses to monocular full – field stimulation are the (1) P100 latency at the mid occipital (MO) site and amplitude of the P100 component at all three occipital sites . Additional latency , duration and amplitude measures generally add little to clinical interpretation . Abnormality may present as changes in latency , amplitude , topography and waveform . P100 latency prolongation is the most reliable indicator of clinically significant abnormality, being least affected by technical factors and degree of patient cooperation .

Amplitude and topographic measures are closely related and may be indicators of clinical significant abnormality but they are more prone to alteration with technical factors ,patient cooperation, fixation and alertness . So in our study we have taken the most reliable P100 component of visual evoked potentials for analyzing the hypothyroids.Waveform abnormalities are generally subjective in nature and difficulty to quantify . Further each laboratory performing VEP testing should have its own normative data based on its own stimulating and recording equipment and guidelines .It is found normative data vary with age and gender **Chatrian et al (1980)** says that the apparent effects of gender on latency values may actually be determined by head size. [29,31] Monocular latency abnormality indicates a unilateral optic nerve dysfunction and bilateral latency abnormality suggests bilateral visual dysfunction. Hypothyroidism has been reported to affect both the electroencephalogram (EEG) and the visual evoked potential (VEP) to flash stimulation[32].The function of central visual pathway was evaluated by pattern VEP [33]. According to **El-Salem K et al (2006)** , the slowing of conduction velocity or prolongation of latency usually implies defects in myelination and loss of amplitude due to axonal dysfunction [34].

Calcium, the most abundant cation in the body and establish powerful homeostatic mechanisms by maintaining circulating ionized calcium levels.[35] The hormones - Calcitriol , Parathyroid hormone , Calcitonin regulates plasma calcium within normal range. The normal concentration of serum calcium is 9-11 mg/dl. About half of this (5mg/dl) is in ionized form which is functionally most active. At least 1mg/dl of calcium is found in association with citrate or phosphate. Other half is bound to proteins, mostly albumin,to a lesser extent to globulin. Ionised and citrate bound calcium is diffusible whereas protein bound is non diffusible . In the laboratory determination of serum calcium , all the three fractions are measured.

REGULATION OF CALCIUM



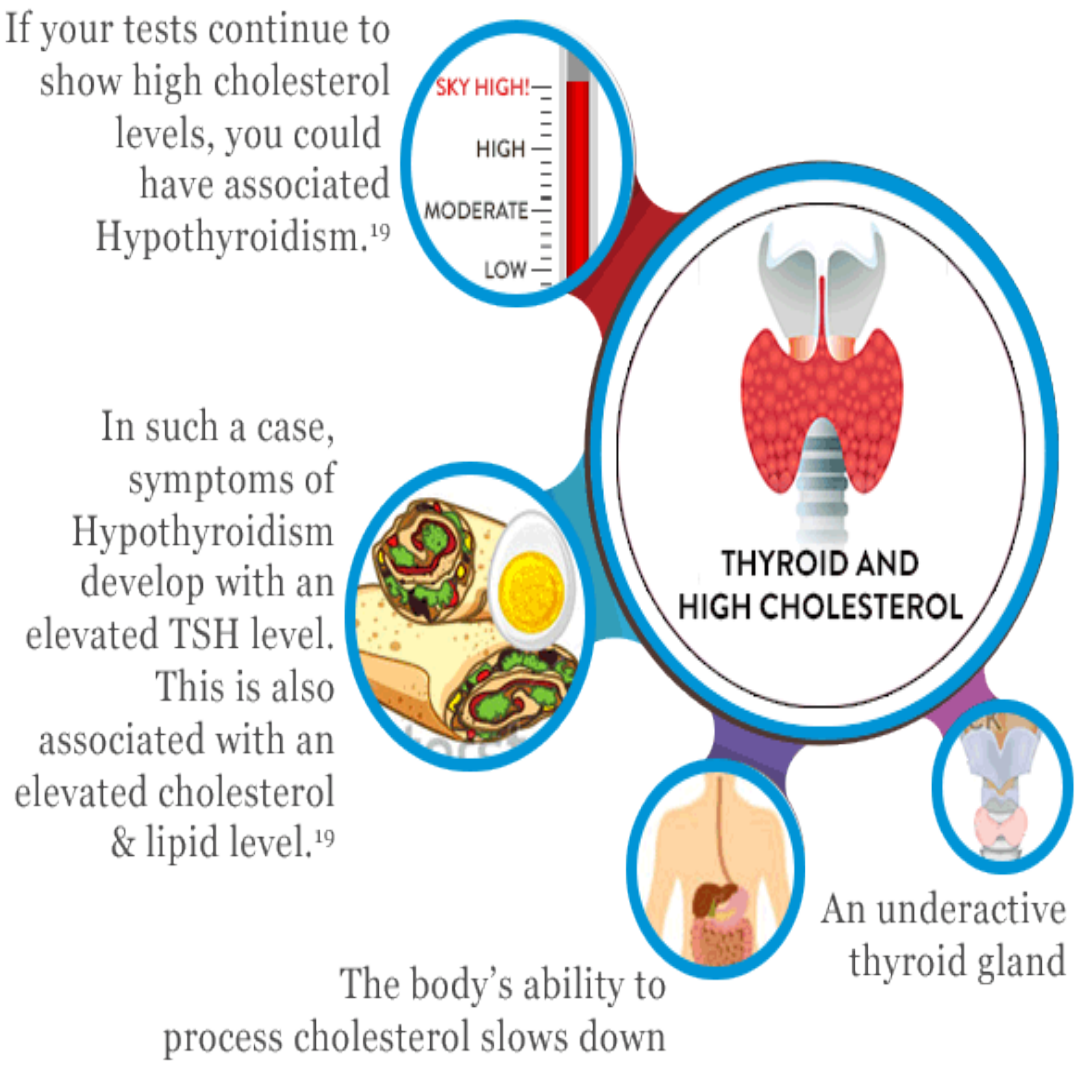
Calcium facilitates the release of hormones like PTH , calcitonin , insulin from endocrine glands[36] . Thyroid disorders are important cause of secondary osteoporosis [37.] **. Rizzoli R , Sato K et al** says that serum calcium and phosphorus levels could be fairly used as index of bone resorption. Thyroid hormones exert its effect on osteoblasts via nuclear receptors to stimulate osteoclastic bone resorption [38,39] . In hypothyroidism , there is increased production of calcitonin and can promote the tubular reabsorption of phosphate and also favors the tubular excretion of calcium.[40]. According to **Biondi B , Cooper DS et al** bone remodeling is affected by the direct or indirect effect of the thyroid hormones on bone cells [41] **.** Bone is affected by the interaction of thyroid stimulating hormone (TSH) with the TSH receptors that are expressed on the precursors of osteoblasts and osteoclasts.[42] . **Huerta MG, Hussein et al** says that studies revealed that metabolic syndrome and cardio vascular diseases were related to disturbance in metabolism and calcium in hypothyroidism. [43 , 44]

Thyroid hormone performs a role in hemoglobin synthesis in adults and maturation of hemoglobin in fetus and hypothyroidism leads to anemia via reducing the oxygenation process through disturbing hematopoietic process **(Chu JY , Franzese AY , Lippi G et al)** [45,46,47] . Iron is consider to be one of the important element that is require in metabolism of thyroid hormone [48] .

Kammal M , Abdrabo AA et al says that Iron acts as a cofactor which catalyse the activity of various important biological enzymes including TPO [49] . This unique enzyme involved in the catalization of first two reaction of thyroid hormone biosynthesis[50] . **Akhter S , Nahar ZU et al** says that this acts as a membrane bound enzyme responsible for oxidation of iodide and binding of iodine to tyrosyl residue of thyroglobulin [51]. Iron is stored in the spleen, liver and bone marrow in the form of ferritin. Ferritin is the temporary storage form of iron in the mucosal cells. Ferritin is colourless and is finely dispersed in tissues ,which is not ordinarily visible microscopically . But when present in large quantities , it gives faint bluish tint to tissues stained for iron by ferrocyanide method . Ferritin composed of a spherical outer shell of an iron - free protein , apoferritin and an inner core of trivalent iron . Apoferritin is made up of 24 subunits . Iron passes in and out of the cell through 6 channels. A molecule of apoferritin (mol. Wt. 500,000) can combine with 4000 atoms of iron .The maximum iron content of ferritin on weight basis is around 25% **(U.Satyanarayana et al (2004)** .An immunoradiometric (labeled antibody) assay for measuring serum ferritin concentration was first established by **Addison et al (1972).** Normally serum ferritin is stable and shows little diurnal variation. Its concentration is related to body iron stores and is age and sex dependent . **De Gruchy (1994) et al** says that serum ferritin concentrations

in adults range between 15 and 300 µg /l and the mean level in men and women are 123µg/l and 56µg/l . Serum ferritin level of 12µg/l or less is diagnostic of iron deficiency [52].

HYPERLIPIDEMIA IN HYPOTHYROIDISM



According to **Brites FD , Bonavita CD et al** there is a strong association between the risk of coronary artery disease (CAD) , high levels of low density lipoprotein (LDL) cholesterol, and low levels of high density lipoproteins (HDL-C) cholesterol has been well established [53] . Thyroid hormones stimulates every aspects of lipid metabolism which includes synthesis, mobilization and degradation. Liver is the main organ for cholesterol synthesis. 3-Hydroxy-3-Methyl-Glutaryl Coenzyme A Reductase (HMGCR) is rate limiting enzyme for cholesterol synthesis ,regulated by various hormones like insulin, glucocorticoid , estrogen , glugogan and thyroid hormones. [54] **(Muller R , Liu YY et al)** . According to **Ness GC , Chambers CM et al** in hypothyroidism HMGCR mRNA levels are reduced and treatment with thyroid hormone restores it to normal level. Thyroid hormone stimulates HMGCR transcription and increases its stability [55] . **Goldstein JL, Bakker O , Lopez D , Huuskonen J et al** said that HMGCR stimulation occurs via Sterol Regulatory Element Binding Protein -2 (SREBP-2) , a cholesterol sensing factor , low density Lipoprotein Cholesterol Receptor (LDL-R) and ATP - Binding Cassette Transporters (ABCA1 and ABCGS/8) [56,57,58,59,60] . According to **Shin DJ, Osborn TF et al** , thyroid hormone stimulates SREBP2 gene when intracellular cholesterol is low leading to increasing SREBP2-mediated HMGCR gene transcription. Conversion of

cholesterol into bile acids is important to maintain whole body cholesterol homeostasis. Cholesterol 7 hydroxylase (CYP7A1) ,a rate limiting enzyme for bile acid synthesis is regulated by thyroid hormone [61] . According to **Lithell H , Kuusi T ,Tan KC et al** , thyroid hormone increases the activity of the enzymes involved in the metabolism of lipoproteins and reverse cholesterol transport such as hepatic lipase (HL) , liprotein lipase (LPL), cholesteryl Esters Transfer Protein (CETP) and Lecithin-Cholesterol Acyltransferase (LCAT) [62,63,64,65] .So dyslipidemia found to be a common metabolic abnormality in patients with thyroid disease , either in the overt or subclinical forms of the disease .According to **Nikkila EA , Abrams JJ et al** , LPL is an essential enzyme responsible for removing triglycerides (TG) from circulating chylomicrons and very low density lipoproteins (VLDL). LPL catalyses TG breakdown into non esterified fatty acid and transporting to adipose tissue where it re-esterified and storage as TG [66,67]. As per **Colorado Thyroid Disease Prevalence Study**, there is gradual increase in fasting total cholesterol , LDL-C and triglyceride levels as thyroid function declined [68]. Metabolic syndrome is a state in which most features of hypothyroidism are seen . Modified National Cholesterol Education Program's Adult Treatment Panel III (NCEP-ATP III) for metabolic syndrome includes elevated fasting glucose , hypertriglyceridemia , hypertension, low serum

HDL cholesterol and increased waist circumference [69] . **Cappola AR , Ladenson PW et al** says that hypothyroidism found to be associated with obesity , dyslipidemia and high risk of atherogenic cardiovascular diseases[70] Lifestyle changes over the last century , including reduced physical activity , increased calorie consumption ,frequent exposure to stress found to play a key role in obesity . Thyroid disorders found to associate with body weight and subclinical hypothyroidism associated with weight gain frequently .Also association between thyroid hormones and resting energy expenditure are established well and there is an inverse relationship between obesity and resting energy expenditure (REE) . REE based on obligation and adaptive thermogenesis and it is under control of T_3 and thyroid hormone[71]. Thyroid hormone stimulate change in physical activity which alters the body mass and the TSH levels usually correlate with body weight [72,73] **(Roel Fsema F , Dall's asta C et al) .** According to **Astrup et al (1996),** thyroid hormones are the main regulators of the body's metabolic rate have a profound effect on weight by increasing enzyme levels in the cell ,mitochondria which produce energy , thyroid hormones control how the body burns up carbohydrates and fats [74] . Weight gain ,a classic symptom of thyroid dysfunction , also causes elevation of TSH in an attempt to raise the production and secretion of thyroid hormones from thyroid gland[75] . Another mechanism contributing to

weight gain in hypothyroidism is the accumulation of fluid rich in glycosaminoglycans. **Van den Beld AW , Visser TJ (2005) et al** said that elevated TSH in obese individuals is due to a neuroendocrine dysfunction caused by deregulation of the hypothalamo pituitary axis[76] .The WHO and the National Heart Lung and Blood Institute of Health advocated the use of a specific BMI threshold of 30 to diagnose obesity and 25 to diagnose overweight [77,78]

WHO criteria for obesity and BMI associated disease risk

CRITERIA	**OBESITY CLASS**	**BMI (Kg/m2)**	**RISK**
Underweight		<18.5	Increased
Normal		18.5 – 24.9	Normal
Overweight		25 – 29.9	Increased
Obesity	I II	30 – 34.9 35 – 39.9	High Very High
Extreme obesity	III	>40	Extremely High

Additional risk :

- **Waist circumference >40 inches in men and >35 inches in women**
- **Weight gain >5Kg since age 18-20**
- **Poor aerobic fitness and Southeast Asian descent**

Indian classification of Obesity

BMI (Kg/m2)	Classification
18.5 - 22.9	Normal
23.0 - 24.9	Overweight
25.0 – 29.9	Obese

Obesity reveals energy intake from foods exceeding energy expenditure by physical activity[79] **(J.O.Hill , H.R.Wyatt (2003) et al).** Recent evidence suggests that thyroid hormones may access the arcuate nucleus and other regions of the hypothalamus to regulate apetite [80] **(Amin A , Dhillo W.S. (2011) et al).**

MATERIALS AND METHODS

MATERIALS AND METHODS

Study design:

It is a cross sectional observation study

Place of study:

The study was conducted in Tirunelveli Medical College Hospital , Tirunelveli.

Collaborating department:

Department of Biochemistry,Tirunelveli medical college,Tirunelveli.

Department of Medicine,Tirunelveli medical college,Tirunelveli.

Department of Neurology ,Tirunelveli medical college ,Tirunelveli

Period of study:

2 years (December 2015 – July 2017)

Study subjects :

100 subjects (50 cases + 50 controls)

Inclusion criteria : Totally 100 subjects , out of which 50 cases of newly diagnosed hypothyroids & 50 cases of non hypothyroids (controls) of age

group 20 - 50 years in both genders . The diagnosis of hypothyroidism was based on laboratory criteria of decreased serum total T_4 associated with increased TSH (>10µIU /ml) .

Exclusion criteria :

Age less than 20 years & greater than fifty years , known malignancy, acute or chronic systemic illness , liver & kidney disorders , Ocular and retinal disorders, pregnancy, any swelling in neck , those taking medications like thyroxine , lithium , steroids , family history of thyroid disorder.

Materials used for the study :

1. Proforma: To obtain a detailed history , to record the anthropometric measurements of the subjects & the clinical findings.
2. Stadiometer : To measure height in centimeters
3. Portable weighing machine : To record the body weight in kilograms
4. RMS EMG. EP MARK II : Using this machine the visual evoked potentials recorded in both eyes, which is manufactured by RMS recorders and medicare system , Chandigarh.

Methodology :

The study was initiated after getting approval from Instituitional Ethical Committee . The study was carried out in non communicable disease (NCD) outpatient Department of Medicine after explaining the procedures thoroughly and getting written & informed consent from all subjects in regional language (Tamil) as well as in English. Emphasis was given that participation in this study was voluntary.

The experimental protocols involved are ,

Recording of detailed history about their diet , physical activity, sleep duration ,vision , mensural cycles, family history of thyroid disease, cardiovascular disease and diabetes .

PHYSICAL EXAMINATIONS

MEASUREMENT OF BMI PARAMETERS

WEIGHT

HEIGHT

Measurement of anthropometric indices :

Height :

The subjects were instructed to wear cotton clothes. The subjects were asked to stand erect , with their relaxed arms , at their side and with feet together.Using Stadiometer fixed to wall vertical height was measured in centimeters to the nearest 0.5 centimeters .

Weight:

Weight in kilograms was recorded using a portable standard weighing machine. Weight was measured to nearest 0.5 kg in subjects wearing indoor clothing and without shoes.

Body mass index :

Body mass index was calculated using the Quetelet's formula .

$$BMI = \text{Weight (Kg)} \ / \ \text{Height } (m^2)$$

Blood investigations :

Under strict aseptic precautions , about 3ml of venous blood were collected from antecubital vein using 5ml disposable syringes in fasting condition Serum was separated within half an hour by centrifugation and stored at 2 - 8° C temperature till analysis was done .

Biochemical tests :

Thyroid profile :

Serum TSH , Serum total T3 , Serum total T4 were determined by Fully Automated Biochemical Analyser EM 360-60519 and quality control by ERBA norms. Normal values of

$T_3 \rightarrow$ 0.5-2ng/ml ,$T_4 \rightarrow$ 4.4-11.6µg/dl , TSH → 0.5-7µIU/ML

Lipid profile:

Serum total cholesterol, HDL cholesterol and triglycerides were measured using ERBA Biochemical Analyser . LDL cholesterol was calculated by

Friedewald's formula { LDL_C = Total cholesterol − HDL_C – TGL /5}

Normal values of Total cholesterol→150-200mg/dl ,TGL→70-200mg/dl , HDL→35-60mg/dl , LDL→70-130mg/dl

Serum electrolytes

Serum calcium and serum ferritin were measured using ELISA reader - EC31509522 (BIORAD Company) using standard kit (AVANTOR)

The standard kit used for analyzing serum calcium is AGAPPE and the quality control used in serum ferritin is SPINREACT ferritin control (Ref: 1107044) .

Normal value of

Serum Calcium → 9.4-10mg/dl

Serum Ferritin : Males → 20-200µg/dl

Females → 20-110µg/dl

MEASUREMENT OF BMI PARAMETERS

WEIGHT

HEIGHT

COLLECTION OF BLOOD SAMPLES

ELISA READER - EC31509522 (BIORAD COMPANY) USING STANDARD KIT (AVANTOR)

Visual evoked potential

Requirements :

Standard disc EEG electrodes

Preamplifier and amplifier

Oscilloscope

Electrode paste

Instrument:

RMS EMG. EP MARK II manufactured by RMS recorders and medicare system , Chandigarh.

Procedure:

Equipment set up

Montage:

Channel 1 – FPz – Reference Electrode

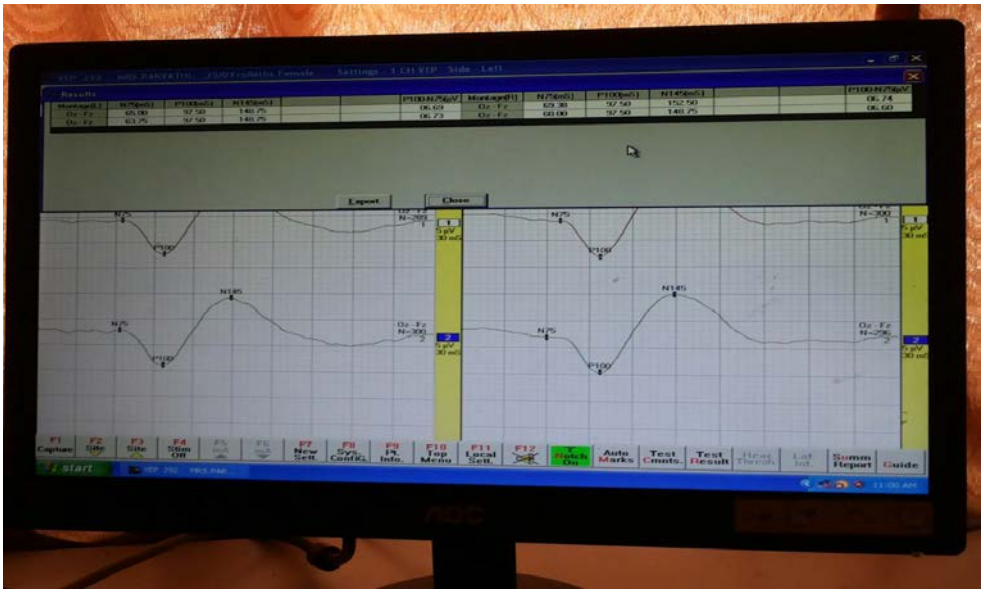
Vertex - Cz – Ground Electrode

C – Oz - Active Electrode

RMS EMG .EP MARK II

PLACING ELECTRODES AND RECORDING OF VEPs

NORMAL P100 WAVE LATENCY OF VEPs



PROLONGATION OF P100 LATENCY (HYPOTHYROIDISM)

Recording condition:

Filter - High filter cut - 100-300hz

Amplification - 20,000-1,00,000

Sweep duration - 300 msec

Number of epochs - 100 (average)

Electrode impedence – Less than 5kilo ohms

Stimulation:

Black & white checker board will be used

Distance between the subject & screen will be 100 cm

Contrast - 80%

Size of pattern - 14 x 16 mins

Rate of stimulation – 4 - 8 hz

Mean luminance of central field 50 cd/m^2

Background luminance - 20-40 cd/m^2

Procedure:

The subject is asked to sit comfortably on a chair with their footwear.

Each eye tested separately .

The other eye is kept covered with an opaque eye shield to prevent the entry of light into that eye .

The skin at the point of placement of electrodes is cleansed with spirit.

The electrodes were placed as per the guidelines and then connected through the preamplifier to the cathode ray oscilloscope .

The subject is instructed to fix gaze at the centre (red box) of the screen.

The visual stimulus is delivered by photostimulator at a frequency of 10 flashes per sec.

VEP parameter measured for the study

Latency of P100 in both right and left eyes of the subject.

ANALYSIS OF RESULTS

Table: 1 - Sex-wise Distribution of the Respondents

Sex	No. of Respondents	Percentage
Male	**12**	**24.00**
Female	**38**	**76.00***
Total	**50**	**100.00**

***Significant**

Out of 50 (N) hypothyroids

12 were males and 38 were females

Males 24%

Females 74%

Hypothyroidism was predominance in females (76%) than males(24% **)**

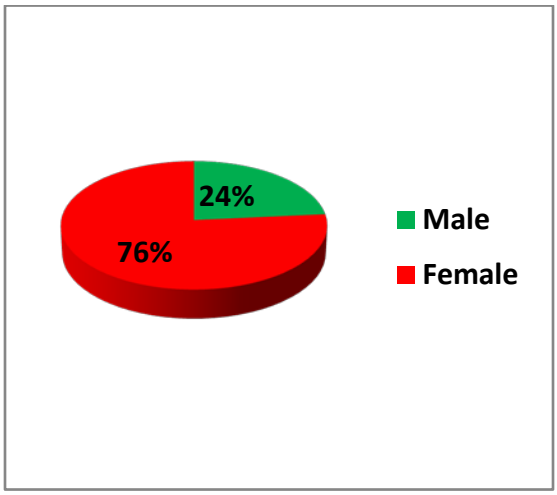


Table: 2 - Age-wise Distribution of the Respondents

Age (in years)	No. of Respondents	Percentage
Below 30	7	14.00
30 - 40	23	46.00*
40 - 50	16	32.00*
Above 50	4	8.00
Total	50	100.00

***Significant**

Mean age distribution was between 32 – 46 years

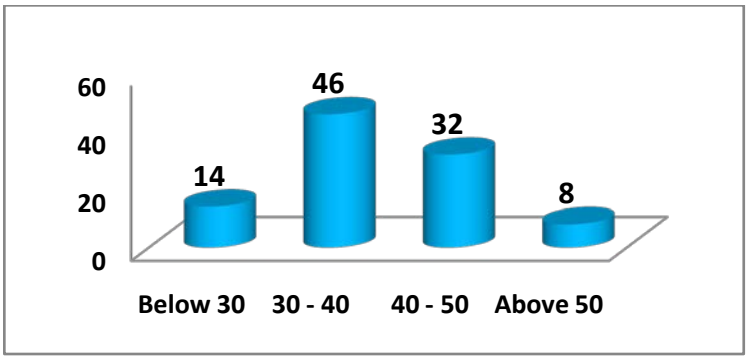
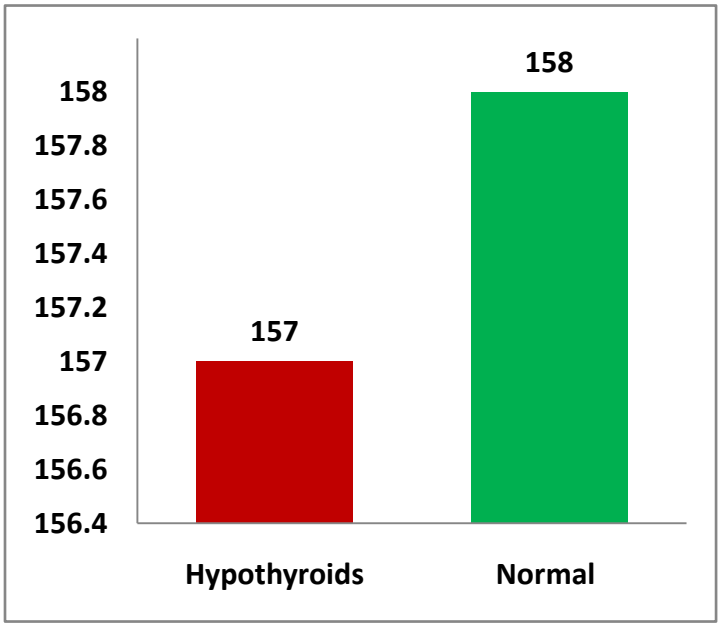


Table: 3 - Height-wise Distribution of the Respondents

Height (in cm)	No. of Respondents	
	Normal	Hypothyroids
Below 150	9 (18)	7 (14)
150 - 166	33 (66)	37 (74)
Above 166	8 (16)	6 (12)
Total	50 (100)	50 (100)



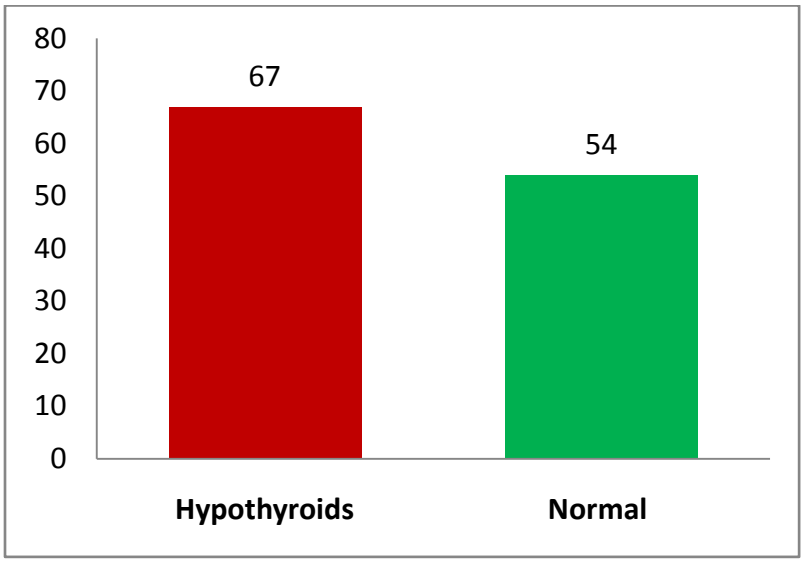
Pearson's correlation showed less significance 'r' value (0.98)

Table: 4 - Weight-wise Distribution of the Respondents

Weight (in kg)	No. of Respondents	
	Normal	Hypothyroids
Below 51	11 (22)	1 (2)
51 - 63	31 (62)	17 (34)
Above 63	8 (16)	32* (64)
Total	50 (100)	50 (100)

***Significant**

Pearson's correlation showed highly significant 'r' value (0.26)



Mean weight variation of hypothyroids (67Kg) and controls(54Kg)

Table: 5 – Body Mass Index (BMI)

BMI (in Kg/m2)	No. of Respondents	
	Normal	Hypothyroids
Below 22	16 (32)	0 (0)
22- 24	28 (62)	5 (10)
Above 24	6 (16)	45* (90)
Total	50 (100)	50 (100)

***Significant**

Out of 50 hypothyroids

BMI > 24Kg/m2 → 90%

BMI between 22-24Kg/m2 →10%

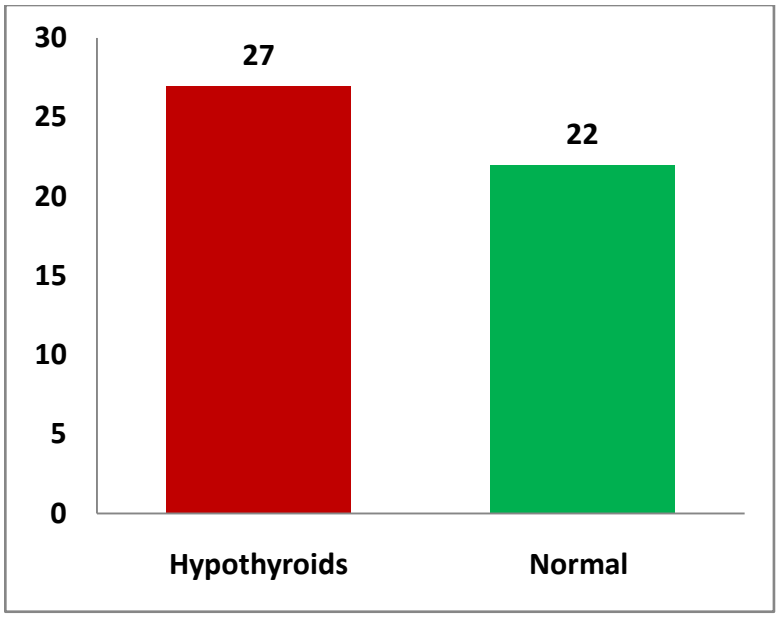
BMI<22Kg/m2 →0%

P value < 0.05 is significant

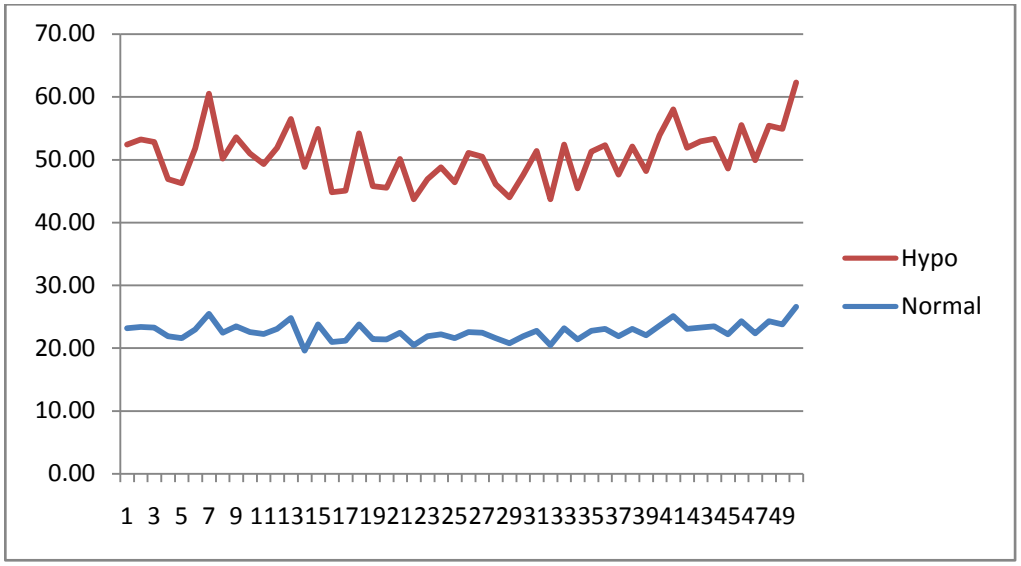
One sample 't' test showed significant P value <0.031

Pearson's correlation showed significant 'r' value (0.91)

Mean BMI of hypothyroids (27Kg/m2) and controls (22Kg/m2)



Mean BMI of hypothyroids (27Kg/m2) and controls (22Kg/m2)

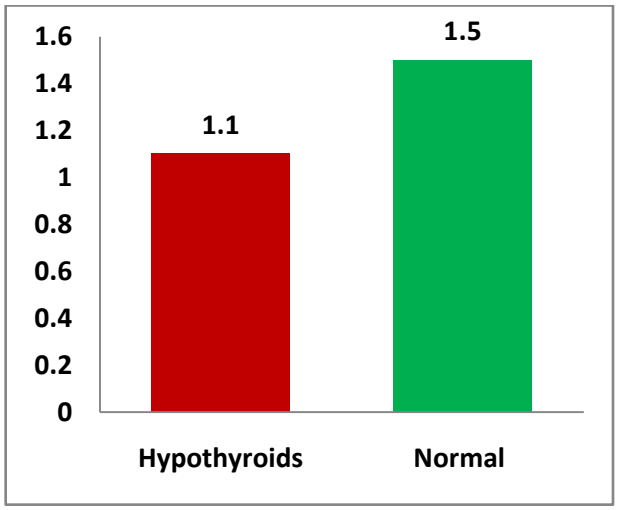


The trend line showed BMI of hypothyroids was higher than the controls

Table: 6 – Triiodothyronine (T3)

SerumT3 (in ng/ml)	No. of Respondents	
	Normal	Hypothyroids
Below 1.3	5 (10)	26* (52)
1.3 – 1.9	44 (88)	21 (42)
Above 1.9	1 (2)	3 (6)
Total	50 (100)	50 (100)

***Significant**



One sample 't' test reveal significant Pvalue (0.000)

Pearson's correlation showed significant 'r' value (0.91)

Table: 7 – Thyroxine (T4)

T4 (in µg/dl)	No. of Respondents	
	Normal	Hypothyroids
Below 6.9	9 (18)	34* (68)
6.9 – 11.2	30 (60)	14 (28)
Above 11.2	11 (22)	2 (4)
Total	50 (100)	50 (100)

***Significant**

Out of 50 hypothyroids , 68% (N=34) had T4 below 6.9 µg/ml

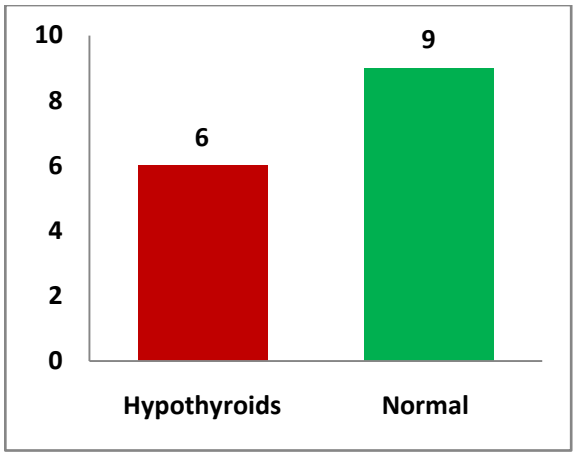
28% (N=14) were between 6.9-11.2 µg/ml

4% (N=2) were above11.2µg/ml

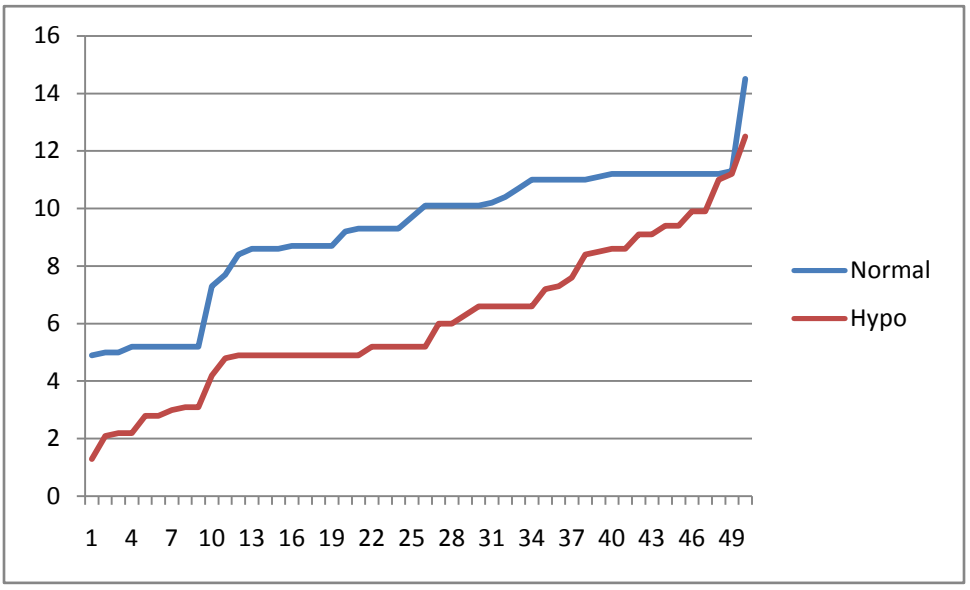
P value < 0.0001 denotes highly significant

One sample 't' test showed significant P value (0.000)

Pearson's correlation showed significant 'r' value (0.91)



Mean value of T4 in hypothyroids (5µg/ml) and controls (9µg/ml)



The trend line showed that T4 in lower in hypothyroids than the controls

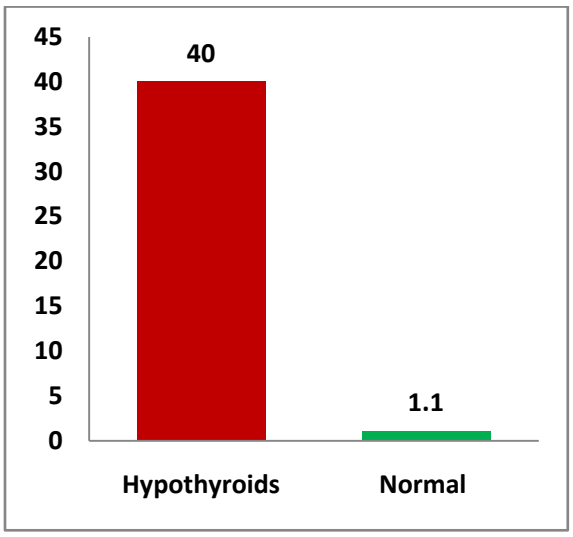
Table: 8 –THYROID STIMULATING HORMONE (TSH)

TSH (in µIU/ml)	No. of Respondents	
	Normal	Hypothyroids
Below 0.04	0 (0)	0 (68)
0.04 – 2.09	43 (86)	0 (0)
Above 2.09	7 (14)	50* (100)
Total	50 (100)	50 (100)

***Significant**

One sample 't' test showed highly significant P value (0.000)

Pearson's correlation analysis showed significant 'r' value (0.69)



Mean TSH value higher in hypothyroids (40µIU/ml) than controls (1.1µIU/ml)

Table: 9 – FERRITIN

FERRITIN (in µg/l)	No. of Respondents	
	Normal	Hypothyroids
Below 75	6 (12)	48* (96)
75 – 89.3	27 (54)	1 (2)
Above 89.3	17 (34)	1 (2)
Total	50 (100)	50 (100)

***Significant**

One sample ‘t’ test showed highly significant P value (0.000)

Pearson’s correlation analysis showed significant ‘r’ value (0.81)

Mean ferritin in hypothyroids (40.6µg/l) is lower than controls(82.9µg/l)

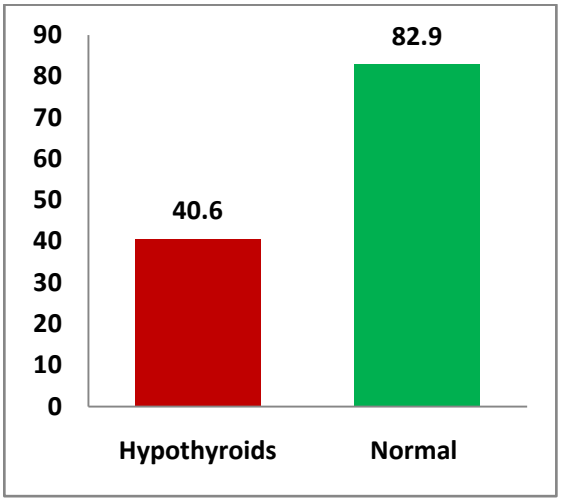


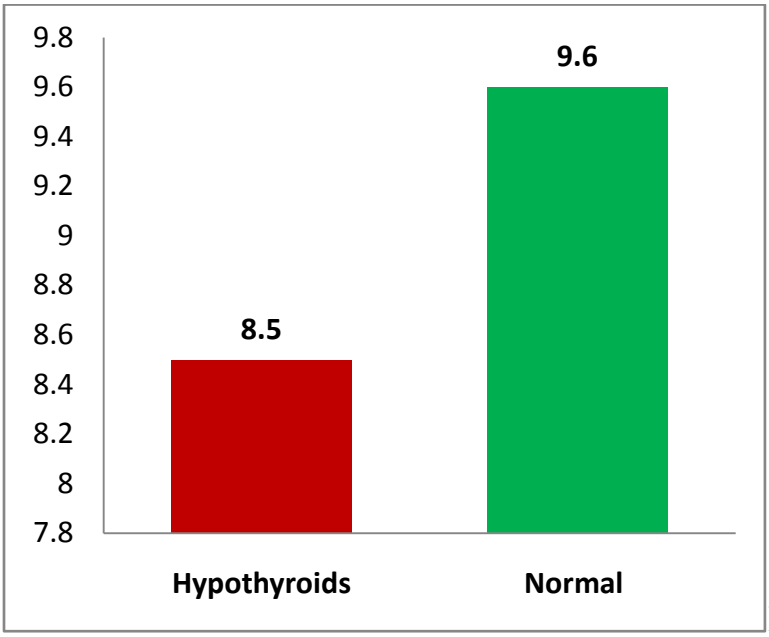
Table: 10 – CALCIUM

Calcium (in mg/dl)	No. of Respondents	
	Normal	Hypothyroids
Below 9.2	0 (0)	24* (48)
9.2 – 10	26 (52)	9 (18)
Above 10	24 (48)	17 (34)
Total	50 (100)	50 (100)

***Significant**

One sample't' test showed highly significant P value (0.001)

Pearson's correlation showed significant 'r' value (0.86)



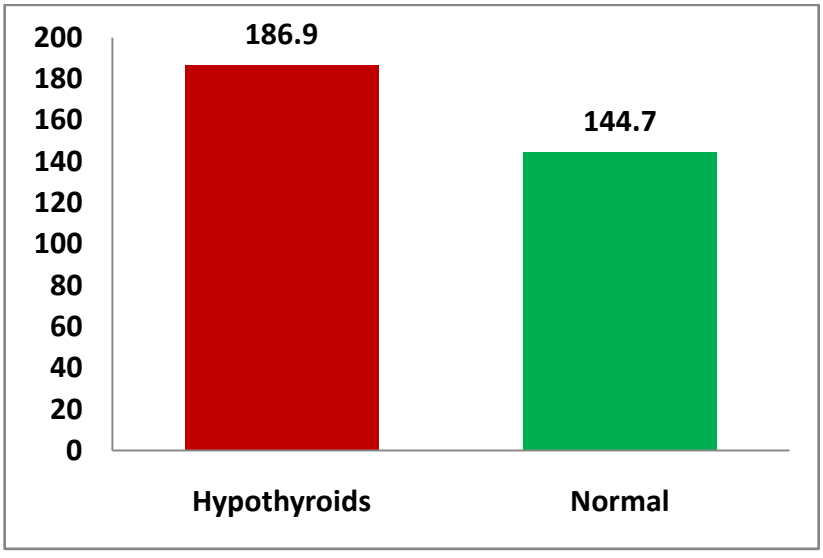
Mean calcium in hypothyroids (8.5mg/dl) was lower than the controls (9.6mg/dl)

Table: 11- T.CHOLESTEROL

T.CHOLESTEROL (in mg/dl)	No. of Respondents	
	Normal	Hypothyroids
Below 133	8 (16)	7 (14)
133 – 156.5	26 (52)	8 (16)
Above 156.5	16 (32)	35* (70)
Total	50 (100)	50 (100)

***Significant**

One sample't' test showed highly significant P value (0.000) Pearson's correlation showed significant 'r' value (0.89)



Mean cholesterol was higher in hypothyroids (186.9 mg/dl) than controls (144.7mg/dl)

Table: 12 – TRIGLYCERIDES (TGL)

TGL (in mg/dl)	No. of Respondents	
	Normal	Hypothyroids
Below 154.2	9 (18)	3 (6)
154.2 – 177.1	20 (40)	30 (60)
Above 177.1	21 (42)	17 (34)
Total	50 (100)	50 (100)

One sample ‘t’ test showed less significant P value (0.766)

Pearson’s correlation analysis showed significant ‘r’ value (0.73)

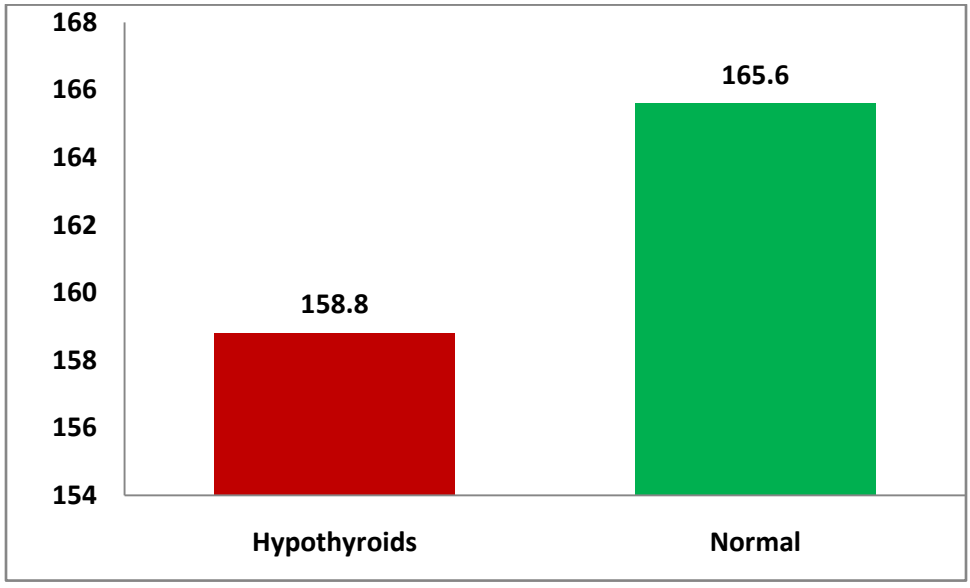


Table: 13 –HIGH DENSITY LIPOPROTEINS (HDL)

HDL (in mg/dl)	No. of Respondents	
	Normal	Hypothyroids
Below 32.2	9 (18)	10 (20)
32.2 – 41.9	30 (60)	12 (24)
Above 41.9	11 (22)	28* (56)
Total	50 (100)	50 (100)

***Significant**

One sample't' test showed highly significant P value (0.004)

Pearson's correlation analysis showed significant 'r' value (0.79)

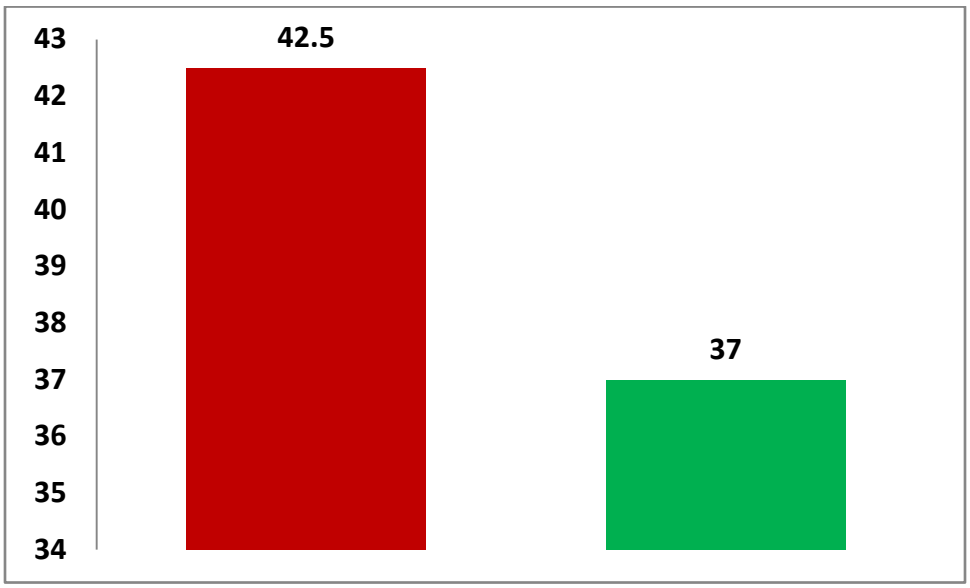
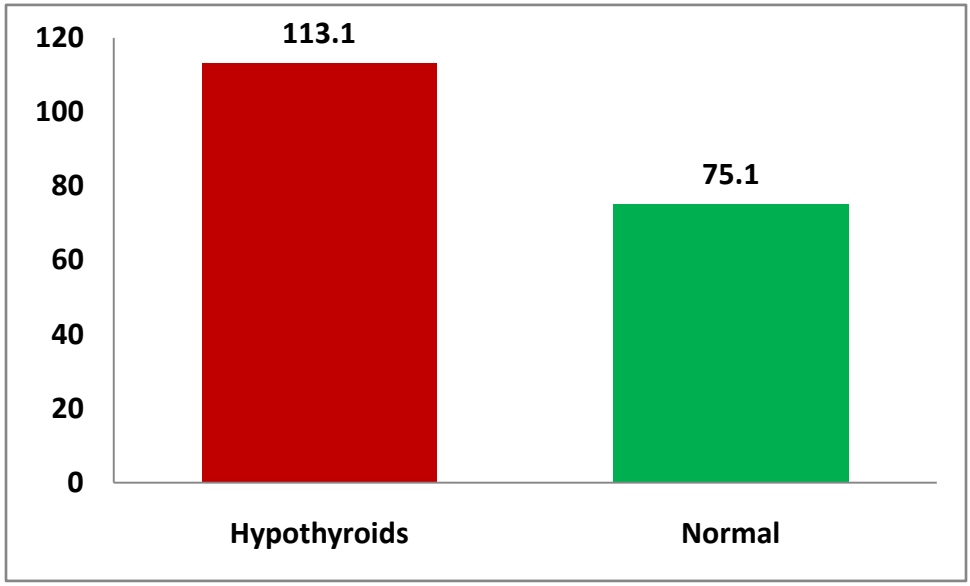


Table: 14 – LOW DENSITY LIPOPROTEINS (LDL)

LDL (in mg/dl)	No. of Respondents	
	Normal	Hypothyroids
Below 67.3	5 (10)	10 (20)
67.3 - 83	32 (64)	36 (72)
Above 83	13 (26)	4 (8)
Total	50 (100)	50 (100)

One sample 't' test showed highly significant P value (0.000).

Pearson's correlation analysis showed significant 'r' value (0.970)



The trend line showed that LDL in hypothyroids was higher than controls

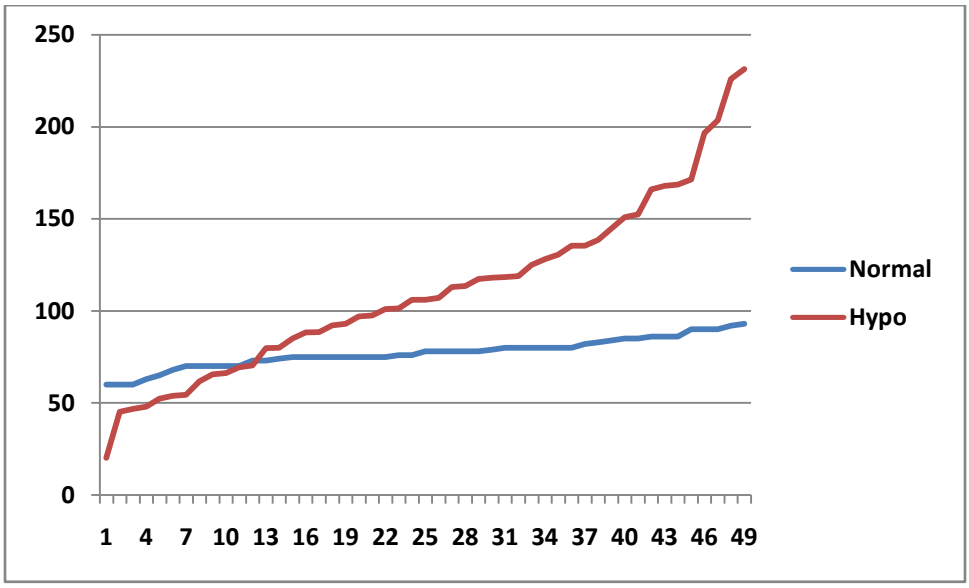


Table: 15 – VISUAL EVOKED POTENTIALS (LT)

VEP (LT) (P100)	No. of Respondents	
	Normal	Hypothyroids
Below 93.7	0 (0)	2 (4)
93.7 – 96.9	7 (14)	6 (12)
Above 96.9	43 (86)	42 (84)
Total	50 (100)	50 (100)

One sample't' test showed highly significant P value (0.000)

Pearson's correlation analysis showed significant 'r' value (0.83)

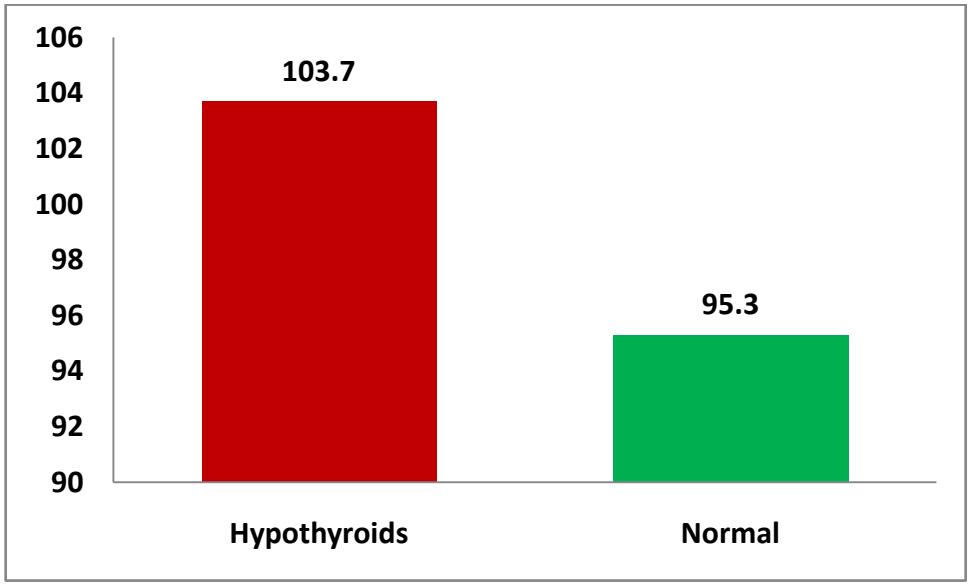


Table: 16 – VISUAL EVOKED POTENTIALS (RT)

VEP (RT) (P100)	No. of Respondents	
	Normal	Hypothyroids
Below 94.5	0 (0)	3 (6)
94.5 – 96.6	2 (4)	6 (12)
Above 96.6	48 (96)	46 (92)
Total	50 (100)	50 (100)

One sample ‘t’ test showed highly significant Pvalue (0.000)

Pearson’s correlation analysis showed significant ‘r’ value (0.9)

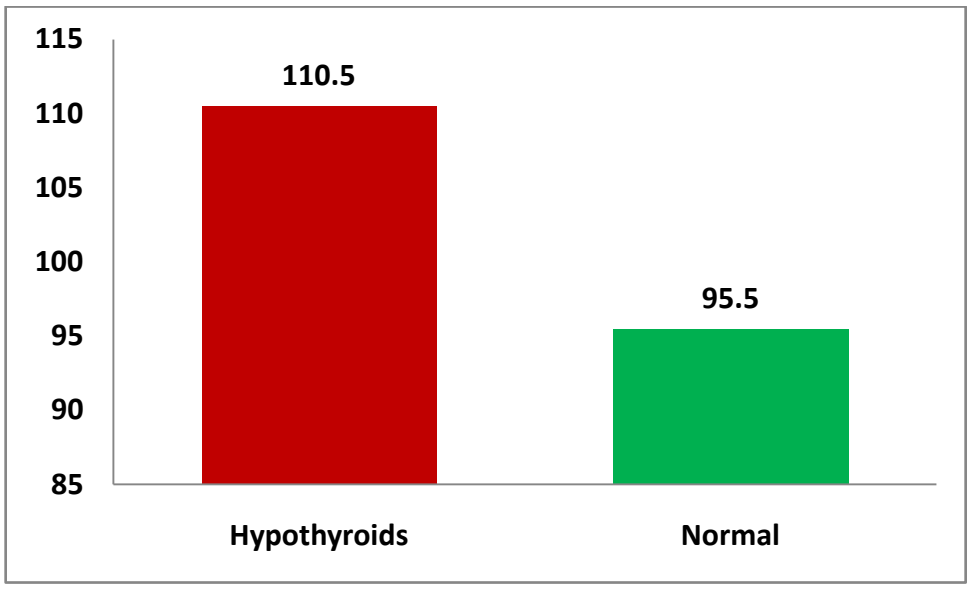


Table : 17 - VEP (LT) and VEP(RT)

	't' Value	**P - value**
VET(LT) and VEP(RT)	**2.424**	**0.019**

Paired 't' test of P100 latency of right and left eyes showed significant P value (0.019).

In hypothyroidism , P100 latency of VEPs in both eyes showed a mild prolongation /delay when compared to the control .P100 latency of right eye was more prolonged than left eye.

Table:18

Pearson's Correlation Analysis – Normal vs Hypothyroid

	'r' Value
HT	**0.98**
WT	**0.26**
BMI	**0.91**
T3	**0.91**
T4	**0.91**
TSH	**0.69**
FERRITIN	**0.81**
CALCIUM	**0.86**
T.CHOLESTEROL	**0.89**
TGL	**0.73**
HDL	**0.79**
LDL	**0.97**
VEP(LT)	**0.83**
VEP(RT)	**0.93**

Pearson's correlation analysis performed on various parameters between hypothyroids and controls revealed significant 'r' values thereby expressing positive or negative correlation .

Table: 19

One Sample 't' Test – Hypothyroid Mean Vs Population Mean

	't' Value	**P - value**
BMI	**2.225**	**0.031***
T3	**4.800**	**0.000****
T4	**7.845**	**0.000****
TSH	**14.736**	**0.000****
FERRITIN	**14.990**	**0.000****
CALCIUM	**3.884**	**0.001***
T.CHOLESTEROL	**5.124**	**0.000****
TGL	**0.299**	**0.766**
HDL	**3.025**	**0.004***
LDL	**5.304**	**0.000****
VEP(LT)	**8.241**	**0.000****
VEP(RT)	**11.565**	**0.000****

***Significant , **Very highly Significant**

P value <0.05 is significant

P value <0.0001 is highly significant

One sample 't' test performed on various parameters between hypothyroids and controls revealed significant P values.

Table 20

One `way ANOVA

ANOVA

HY-VEPL

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	5271.908	46	114.607	27.090	.010*
Within Groups	12.692	3	4.231		
Total	5284.599	49			

Association between hypothyroidism and Visual Evoked potentials using One Way ANOVA test showed significance (0.010)

Tables : 21

Correlation between Serum Calcium and TSH

Pearson Correlation	**'r' Value**	**Sig.**	**N**
Serum Calcium and TSH	-0.224	0.117	50

Pearson's correlation analysis revealed negative correlation between serum calcium and thyroid stimulating hormone (TSH) with 'r' value (-0.224) showing significance (0.117).

Table:22

Correlation between Serum Ferritin and Thyroid hormones

Pearson Correlation	**'r' Value**	**Sig.**	**N**
Serum Ferritin and TSH	0.083	0.568	50

Pearson's correlation analysis between serum ferritin and thyroid hormones revealed positive correlation with 'r' value (0.083) showing significance (0.568)

Table : 23

Correlation between BMI and TSH

Pearson Correlation	**'r' Value**	**Sig.**	**N**
BMI and TSH	0.344	0.014	50

Pearson's correlation analysis between Body mass index (BMI) and Thyroid stimulating hormone (TSH) revealed positive correlation (0.344) with 'r' value showing significance (0.014)

Table : 24

Correlation between Lipids and TSH

Pearson Correlation	**'r' Value**	**Sig.**	**N**
Lipids and TSH	0.062	0.670	50

Pearson's correlation analysis between lipids and thyroid stimulating hormone (TSH) revealed positive correlation (0.062) with 'r' value showing significance (0.670)

DISCUSSION

DISCUSSION

Hypothyroidism is defined as the primary failure of thyroid gland or insufficient stimulation of thyroid gland by the hypothalamus or pituitary gland which leads to reduction in secretion of thyroid hormones to meet the metabolic demands of the body. Primary gland failure may result from congenital abnormalities ,autoimmune destruction (Hashimoto disease) ,iodine deficiency and infilterative diseases.[81] It is said that iodine deficiency is the most common cause of hypothyroidism world wide whereas in iodine sufficient areas autoimmune disease especially Hashimoto thyroiditis and iatrogenic causes is more common . Prevalence increases with age and it is higher in females when compared to males[82] . According to datas derived from **National Health and Nutrition Examination Survey (NHANESIII)** about one in 300 persons in United States has hypothyroidism [83].Evidences said that nearly 13 million Americans have undiagnosed hypothyroidism[84] **(Holfand M (2004) et al) .** If this be the scenario in developed countries then what will be the scenario in developing country like India ? . About 4.2 crores Indians found to suffer from hypothyroidism and symptoms of hypothyroidism are usually confused with other diseases and majority of hypothyroids remain undiagnosed [2] **(The Times of India ,Aug 30, 2017)** . This study was conducted to analyse visual evoked potentials ,serum calcium ,

serum ferritin and lipid profile in these undiagnosed or newly diagnosed hypothyroids by simple random sampling with the laboratory criteria TSH > 10µIU / ml and decreased serum total T_4 and compared these values with that of the controls . Studies said that the serum TSH test found to be the best laboratory test for assessing thyroid function in diagnosing primary hypothyroidism[85] **(Spencer CA et al)** .

Our cross sectional study was performed in Tirunelveli Medical College in the non communicable disease outpatient department involving 100 subjects (N= 50 hypothyroid cases + N= 50 normal controls) of age group 20-50 years including both genders. According to **Annals of Internal Medicine 2015 (Vol ; 162, No 1)** researches will help clarify the benefits and harms of thyroid screening and also favour better understanding of potential effects and harms of thyroid screening research is needed on the prevalence of unrecognized overt thyroid disease and on effects of treating such patients .As per the study of **Unnikrishnan et al,** " the prevalence of undetected hypothyroidism was 3.47 % that is almost 1/3rd of hypothyroid patients (186 out of 587) were diagnosed for the first time during the course of study-related screening [7] . Statistical analysis was preformed with Software Package for Social Sciences version 11.0 (SPSS 11.0). The statistical tests utilized in our study were Paired ' t ' test , Pearson's correlation test , One

sample ‘t’ test , One way ANOVA test .The level of significance chosen for the study was 5% ($P<0.05$). P value <0.0001 was highly significant.

Demographic Profile

In our study, the comparison between sex wise distribution of Hypothyroids and normal controls was shown (Table 1) .Our study observed that there was higher prevalence of hypothyroidism among females (76%) when compared to males (24%). Our findings were correlated with the study of findings of **Naved Ahmad , Meenakshi Panthari et al** whom revealed that hypothyroidism was ten times more common in women than men and also its prevalence increased with age [86].Literature says that higher prevalence of thyroid disorder in females due to estradiol has an antagonistic effect on thyroid hormones T_3 & T_4 and also estradiol competes with T_3 & T_4 for binding sites of receptor proteins **(Vasudevan N (2002) et al)** .Also the findings **of Vanderpump & Tunbridge (1995) , Konno N ,Volzke H , Mason MB , Dunn JT , Monika V , Samuels MH et al** correlated with our findings of female preponderance and increases with age [5,86,87,88,89,90,91,92,].

In the comparison between age wise distribution of hypothyroids and normal controls (Table 2), it was observed that the prevalence of hypothyroidism increased with age and it also revealed that its prevalence below 30

years was found to be 14% (N=7) , 46% (N=23) were between 30-40years , 32% (N=16) were between 40-50years and 8% were above 50years respectively . So in our study we observed prevalence of hypothyroidism found to be statistically significant in the age group 30-40 years (46%) and also in 40-50years (32%).The mean age predominance was between 32-46 years. According to study of **Saha PK , Baur B, Gupta S et al ,** hypothyroidism found to be more prevalent (40.5%) in the age group of 36-45 years with female preponderance[93] . Another study revealed the age preponderance of 34 years and above [94] **(Vander pump & Turnbridge (2002) etal).** Our findings also correlate with the findings of the study in Makkah which showed similar age group predominance of 28-52 years on the prevalence of thyroid disorders [95] **(Lamofon HA (2008) etal)** .The comparison of height –wise distribution of hypothyroids and normal controls was observed (Table 3). Our study revealed that about 14% (N=7) of hypothyroids the height was below 150cm, 74% (N=37) had the height variation between 150-166 cm and 12% (N=6) was above 166cm and when compared with the controls the height variations were 18% (N=9) , 66% (N=33) and 18% (N=9) respectively . Hence in our study the mean variation in height between the hypothyroids (157cm) and the controls (158cm) is found to be less significant with 'r' value (0.98) using Pearson's

correlation analysis (Table:18) . Various literature said that thyroid hormones are essential for normal skeletal growth and maturation , formation and eruption of teeth ,ossification of cartilage , normal face contours and for normal body proportions. Thyroxine normally potentiates the pituitary growth hormone effects and has efficient permissive effect on growth hormone .So in hypothyroidism in the young , there will be a growth retardation **(Sarada Subrahmanyam et al (re prin.2014) .**

Weight gain ,a the classical symptom in hypothyroidism. The comparison of weight-wise distribution between hypothyroids and normal controls was noted (Table 4) . Our observations revealed that about 64% (N=32) of hypothyroids had weight above 63Kg , 34% (N=17) of them had weight ranging between 51-63Kg and 2% (N=1) had weight below 51Kg and when compared with the controls the weight variations were about 16% (N=8) , 62% (N=31) and 22% (N=11) respectively. Hence from our study and it is found that the mean weight gain in hypothyroids (67Kg) is highly significant when compared with the controls (54Kg) of same age group with significant 'r' value (0.26) using Pearson's correlation analysis (Table:18). Studies of **Michalaki MA (2006), Rotondi M (2009) et al** focusing whether elevation of body weight related to an underlying thyroid disorder[96,97] . According to **Rosenbaum (2001) et al** , the changes in body weight found to

be associated with alteration in thyroid hormones and and catecholamine secretion[98]. The findings of our study correlate with the findings of **Sari (2003) , Kotkiewski (1997) et al** who said that weight gain was found to be a classic symptom in thyroid disorder and the TSH levels might increase in an attempt to raise the production and secretion of thyroid hormones from its gland.[75,99]. Studies of **Afridi K.A. & Khan A (2004) et al** , revealed that the growing prevalence of hypertension, diabetes mellitus and cardiovascular disease has been tied to excessive weight[100].Evidences suggested that thyroid hormones may influence arcuate nucleus and other regions of hypothalamus which regulate apetite and also obesity associated with the psychosocial morbidity[80,101] **(Amin A & Dhillo (2011) , Baur L.A. (2002) et al)**

Our study compared of body mass index (BMI) between hypothyroids and normal controls (Table 5) and it was found that 90% (N=45) of hypothyroids the BMI was above 24Kg/m2 ,10% (N=5) was between 22-24Kg/m2 and 0% (N=0) was below 22Kg/m2 ,when compared with controls the values of BMI were 6% (N=16), 62% (N=28) and 32% (N=16) respectively .So our study concluded that the BMI of hypothyroids showed statistically significant increase (27Kg/ m2) when compared with the normal controls (22Kg/m2) with significant P value (0.031) using one sample 't' test and Pearson's correlation analysis revealed significant correlation coefficient or

'r' value (0.91) (Table: 18,19) . According to **WHO obesity criteria** , BMI between 18.5-24.9 denotes normal and BMI between 25-29.9 denotes overweight. Hence in our study, the BMI of hypothyroids represents Overweight . Our findings correlate with the findings of **Knudsen N , Laurberg P (2005) et al ,** said that thyroid function (even within normal limit) would be one of several factors contributed to determine body weight in the general population [102] . Studies of **Reineer T (2010) , Roel Fsema F(2009) , Dall 's asta C (2009) et al** revealed that thyroid hormone induces changes in physical activity → body mass changes → change in TSH levels which usually correlate with body weight[13,72,73]

Thyroid Profile

The comparison of serum T_3 values between the hypothyroids and the normal controls was observed (Table 6) . In our study about 52% . (N=26) of hypothyroids had the serum T_3 level below 1.3ng/ml ,42% (N=21) was between 1.3-1.9ng/ml and 6% (N=3) was above 1.9ng/ml when compared with the controls the values were 10% (N=5) , 88% (N=44) and 2% (N=1) respectively . So the values of mean serum T_3 level in hypothyroids (1.1ng/ml) is slightly lowered when compared to the controls (1.5ng/ml) and revealed significant P value (0.000) using one sample 't' test with significant 'r' value (0.91) by Pearson's correlation analysis (Table: 18,19) .

Our findings were consistent with the findings of **Sridevi D , Amrut A Dambai , Sidrah (2016) et al** which said that decrease in T_3 and T_4 and rise in TSH occurs in hypothyroidism. Various literature said that that normally 90% of thyroid hormones secreted will be released as T_4 and 10 % will be released as T_3 and approximately three fourths of circulating T_3 obtained by the peripheral conversion of T_4 which occurs principally in liver and kidneys.

T_4 in plasma (10:1) acts as a prohormone reserve for synthesis of T_3 responsible for various biological activity. Studies of **Stockigt JR (2001) et al** revealed that there are methods to assess free T_3 concentration by direct immunoassay have developed and are currently in use [103]. Literatures revealed that the triiodothyronine (T_3) play a central role in differentiation, development and maintenance of body homeostasis and their actions found to be mediated through intracellular T_3 – receptor proteins (TRs) thereby modulating transcription by specific binding to T_3 - response elements in target genes . Also T_3 found to exert its post transcriptional level thereby regulating expression of various genes.However, serum T_3 measurement ,whether total or free ,has limited utility in hypothyroidism since the levels are often normal due to the hyperstimulation of the remaining functioning thyroid tissue by elevated TSH and to up-regulation of type 2

iodothyronine deiodinase[104] **(Lum SM ,Nicoloff JT Spencer CA(1984) et al)**. So serum T_3 value is of less significance in detecting hypothyroidism.

Serum T_4 values between hypothyroids and normal controls was observed in our study (Table 7) . It revealed that in 68% N=34 of hypothyroids the serum T_4 value was below 6.9µg/dl , 28% (N=14) was between 6.9-11.2µg/dl and 4% (N=2) was above 11.2µg/dl when compared to the controls the serum T_4 value found to be 18% (N=9) ,60% (N=30) and 22% (N=11) respectively . So the mean serum T_4 of hypothyroids was significantly lowered (6µg/dl) when compared to normal controls (9µg/ml) .Findings also revealed statistically significant P value (0.000) using one sample 't' test and significant 'r' value (0.91) using Pearson's correlation analysis (Table18,19) . Primary hypothyroidism become overt when serum TSH level is high and the serum total thyroxine (T_4) or free T_4 level is less than the population reference range. The findings of our study was found to be consistent with the findings of **Naved Ahamed & Meenakshi Panthari et al (2013)** who said that biochemically reduction in T_3 and T_4 concentrations result in hypersecretion of pituitary TSH resulting in amplified rise in serum TSH levels. Further studies of **Galesanu C & Lisnic N (2004) et al** revealed that this was a key laboratory findings, particularly helps in the early detection of thyroid failure [105] . Estradiol limits the thermogenic action of T_4 and

promotes fat storage[106] .Our findings also correlated with the findings of studies of **Sridevi D (2016) , Ashuma Sachdeva(2015) , Niko rostaei Rad (2016) et al** who said that in hypothyroidism there was reduction in T_3 and T_4 along with the elevation of TSH.[107,108,109]

Our study compared the serum Thyroid stimulating hormone (TSH) levels between the hypothyroids and normal controls (Table 8) and it is observed that in 100% (N=50) of hypothyroids , the serum TSH levels were above 2.09 µIU/ml and 0% (N=0 was between 0.04-2.09 µIU/ml when compared to the controls who had serum TSH levels 14 % (N=7) above 2.09 µIU/ml , 86% (N=43) was between 0.04-2.09 µIU/ml and 0% (N=0) was found below 0.04 µIU/ml .So the values of mean serum TSH in hypothyroids (40µIU/ml) was significantly increased when compared to normal controls (1.1µIU/ml) .Results revealed statistically significant P value (0.000) using one sample 't' test and significant 'r' value (0.69) using Pearson's correlation analysis (Table18,19). Our findings are consistent with the findings of **Roopa Murgod & Gladys Soans (2012) & Mukesh G Gohel & Aashka Shah(2014) etal** who said that there was statistically significant decrease in serum T_4 with increase in serum TSH.[110,111]. According to **Janki Pinakin Desai, Uday N Vachhani (2015) et al ,** as thyroid failure progresses , serum free T_4 levels fall , and the findings of elevated TSH and low free T_4 result in

overt hypothyroidism[112]. **Seyad M , Asadollah H , Amir GK (2009) et al** said that TSH play a critical role for the diagnosis of thyroid disorders[113] . According to National Health and Nutrition Examination Survey III, suggested after reanalysis of the data that the serum TSH distribution shifts towards higher concentrations with age [114] **(Surks MI , Hollowell JG (2007) et al).**

Metabolic functions in hypothyroidism

Ferritin is an indicator of body iron stores and its level altered in hypothyroidism **(Dahiyak K ,Verma M (2016) et al)** [115] . In our study , we compared the ferritin level between the hypothyroids and the normal controls (Table 9). Our study revealed that in 96% (N=48) of hypothyroids , the serum ferritin level was below 75µg/l and 2% (N=1) was between 75-89.3µg/l and 2% (N=1) had ferritin level above 89.3µg/l when compared to the controls ,they had 12% (N=6) , 54% (N=27) ,34% (N=17) respectively. Hence the mean serum ferritin level was significantly lowered in hypothyroids (40.6 µg/dl) when compared with the controls (82.9 µg/dl) Our findings revealed statistical significant P value (0.000) using one sample " t' test and significant 'r' value (0.81) using Pearson's correlation analysis (Table:18,19). Hence alterations in serum concentrations of ferritin reflects thyroid function . Findings of our study correlated with the study of **Ashuma Sachdeva &**

Veena singh (2015) et al which revealed that depletion of iron stores will cause reduction in serum FT_3 and serum FT_4 levels[108]. According to **Klausner RD & Rouault TA (1993) et al** , the thyroid peroxidase (TPO) which was a membrane bound glycosylated hemoprotein , which required iron to play a key role in thyroid biosynthesis due to organification [116] . The iron regulatory protein (IRP) or iron responsive element binding protein (IRE-BP) or iron responsive factor (IRF),a trans acting RNA – binding protein had high affinity to iron responsive elements (IREs) found in ferritin and transferring receptor . **Goossen B(1992) et al , Mullner EW (1988) etal and Tang CK (1992) et al** revealed that in iron depleted state ,the IRP binded to IRE in the 5´ - untranslated region (5´-UTR) of ferritin instead of binding to 3´- untranslated region (3´-UTR) of transferring receptor resulting in decreased ferritin translation and decreased transferrin receptor m RNA stability[118,119,120] . Hence receptor regulation attained at post - translational level and found to be independent of new protein synthesis[117,118,119] . Our study also correlated with the findings of **Akhter S (2012) et al , Christ – Crain M (2003) et al** [51,117].

Thyroxine regulates blood calcium normally by releasing calcium from cells thereby regulates calcium. In our study, the serum calcium levels of hypothyroids was compared with normal controls (Table 10). It was found that

about 48% (N=24) of hypothyroids ,the serum calcium level was below 9.2 mg/dl ,18% (N=9) were between 9.2-10mg/dl , 34% (N=17) found to be above 10mg/dl and when compared with the controls the values were 0% (N=0) , 52% (N=26) and 48% (N=24) respectively. So the mean serum calcium level was significantly lowered in hypothyroids (8.5mg/dl) than the controls (9.6mg/dl).Our study also revealed statistical significant P value (0.001) using one sample 't' test with significant 'r' value using Pearson's correlation analysis (Tables:18,19). According to **Rizzoli R (1986) et al, Sato K (1987) et al , Shlomo Melmed (2011) et al,** in hypothyroidism due to less thyroxine level leads to reduced entry into the cells resulting in reduced calcium release and also thyroid hormones exerted its effect on osteoblast through nuclear receptors thereby stimulating bone resorption of osteoclast [38,39,40]. The findings of our study correlated with the studies of **Gammage MD (1986) et al , Shivaleela MB(2012) et al, Suneel B (2011) et al, Christoph Schwarza (2012) et al** who stated that there was significant reduction in serum calcium levels in hypothyroids when compared with controls[120,121,122,123,124].

Thyroid hormones play a significant role in lipid metabolism and its deficiency result in slowing of metabolic functions which lead to hyperlipidemia and atherosclerotic disease .Our study compared the lipid profile of hypothyroids with that of normal controls (Tables – 11,12,13,14).

Our study revealed the serum total cholesterol of 70% (N=35) of hypothyroids were above 156.5 mg/dl ,16% (N=8) of them were between 133-156.5mg/dl ,14% (N=7) of them found to be below 133mg/dl and when compared with the controls the values were 32% (N=16) , 52% (N=26) and 16% (N=8) respectively .The normal values of serum total cholesterol ranges between 150-200 mg/dl .Our study revealed that the values of serum triglycerides ,found to be about 34% (N=17) of hypothyroids were above 177.1mg/dl, 60% (N=30) of them were between 154.2-177.1 mg/dl and 6% (N=3)of them were below 154.2 mg/dl and when compared with the controls the values were 42% (N=21) ,40% (N=29) , 18% (N=9) respectively.

The findings of serum high density lipoproteins (HDL) revealed that about 28% (N=14) of hypothyroids were above 41.9 mg/dl, 24% (N=12)of them were between 32.2 - 41.9 mg/dl and 20% (N=10) of them were below 32.3 mg/dl and when compared with the controls the values of serum triglycerides were 22% (N=11) , 60% (N=30) and 18% (N=9) respectively . Our study also revealed that the values of serum low density lipoproteins (LDL) of hypothyroids found to be about 8% (N=4) were above 83mg/dl ,72% (N=36) of them were between 67.3-83mg/dl and 20% (N=10) of them were below 67.3 mg/dl and when compared with the values of normal controls the values were 26% (N=13) , 64% (N=32), 10% (N=5)respectively.

So our study revealed that the mean serum total cholesterol of hypothyroids (186.9 mg/dl) was significantly elevated when compared with the controls (144.7mg/dl) with statistically significant P value (0.000) using one sample 't' test and the significant 'r' value (0.89) by Pearson's correlation analysis(Table: 18,19).The values of mean serum triglycerides of hypothyroids (158.8mg/dl) was slightly lowered or normal on comparing to controls (165.6mg/dl) and was found to be statistically less significant with P value (0.766) using one sample 't' test and the significant 'r' value being (0.89) by Pearson's correlation analysis (Table: 18,19) .The values of mean serum HDL of hypothyroids (42.5 mg/dl) was significantly elevated when compared to the controls(37mg/dl) . Hence the results revealed that the statistically significant P value (0.004) using one sample 't' test and the significant 'r' value was 0.73 by Pearson's correlation analysis (Table18,19) . The values of mean serum LDL of hypothyroids (113.1mg/dl) was significantly elevated when compared to the controls (75.1mg/dl) which showed statistical significant P value (0.000) using one sample't' test and significant 'r' value (0.97) by Pearson's correlation analysis (Table 18,19) . Our study correlated wlth the studies of **Roopa Murgod (2012) et al , Chan Hee Jung (2003) et al , Lia Scarabottolo(1986) et al , Jiskra (2007) et al** which revealed that the serum total cholesterol, serum LDL ,serum HDL

were increased in overt hypothyroidism due to the expression of LDL receptors modulated by thyroid hormones[110,125,126,127,]. In overt hypothyroidism, the number of LDL receptors in the liver decreased and as a resulting in an increase in overall cholesterol and LDL cholesterol[126,127] .HDL is increased in hypothyroidism due to reduced activities of cholesterol Ester Transfer Pratein (CETP) and hepatic lipase resulting in reduced transport of cholesteryl esters from HDL-2 to very low density lipoproteins (VLDL) and intermediate density lipoproteins (IDL) **(Leonidas HD (2002) et al** [128] . In our study ,the values of mean serum triglycerides was slightly reduced or normal in hypothyroidism which was contradictory to the findings of **Jiskra (2007) et al** who stated that there would be an increase in triglycerides in overt hypothyroidism due to poor clearance of endogenous and exogenous triglycerides [127].The findings of our study was supported by studies of **Pearce EN (2012) et al , Mullur R (2014) et al** , who revealed that the serum levels of triglycerides were normal or slightly increased.[54,129]

Visual Evoked Potentials

The Visual Evoked Potentials (VEPs) are simple noninvasive electrophysiological tests. Our study of VEPs in left eye (Table15) revealed that about 84% (N=42) of hypothyroids, the P100 latency were above 96.9msec , 12% (N=6) of them were between 93.7 - 96.9msec and 4% (N=2)

of them were below 93.7msec and when compared with the normal controls the values of P100 were 86% (N=43) ,14% (N=7) , 0% (N=0) respectively . VEP findings of right eye revealed that about 92 % N=42 of hypothyroids ,the P100 latency was found to be above 96.6msec ,12% N=6 of them were between 93.7-96.9msec and 6% N=3 were below 94.5 msec . P100 latency varied with laboratory control. According to **Shahrokhi (1978) et al** the P100 latency range was $102.3 \pm 5.1\ msec$ and **Misra & Kalita et al** the P100 latency range was $96.9 \pm 3.6\ msec$ [132] . A latency difference of greater than 10 msec between two eyes is considered significant[33] . Our study revealed statistical significant difference in mean P100 latency between the hypothyroids (103.7msec) and the controls (95.3msec) in left eye with P value <0.000 (Table 19) using one sample 't' test and Pearson's correlation analysis showed significant 'r' value of 0.83 (Table -18,19) .Findings of mean P100 latency in right eye revealed statistically significant difference between the hypothyroids (110.5msec) and the controls (95.5msec) with P value <0.000 (Table19) using one sample ' t' test and Pearson's correlation analysis showed significant 'r ' value of 0.93 (Table18,19). Our study also compared the P100 latency (Table17) between the left eye and right eye using paired 't' test and was found to be statistically significant with P-value (0.019). So our study concluded that there was statistically significant

prolongation of P100 latency in hypothyroids when compared with the controls in both eyes with P value <0.05 .Also our findings revealed that prolongation of P100 latency was more in right eye than the left eye of hypothyroids with significant P value (0.010) using one way ANOVA test (Table:20).Various literature revealed that the prolongation of P100 of cortical wave latency in hypothyroids suggested central nervous system involvement which progressed with the duration of the disease since latency depended on an intact myelinated nerve .According to **El Salem K (2006) etal** slowing of conduction velocity or prolongation of latency or loss of amplitude implied myelination defects and axonal dysfunction and also noticed that 52% of hypothyroids had polyneuropathy [34] . Demyelination in hypothyroidism occurred due to oxidative damage to myelin membrane and oligodendroglial cells . The findings of our study correlated with the studies of **Sankareswari A (2016) et al, Gowri Velayutham (2012) et al** , **El-Salem K (2006) et al** , **Jayanthi (2015) et al** whom also revealed that the electrophysiological studies were useful in diagnosing asymptomatic poly neuropathy in hypothyroidism[130,131,132,133]. The p100 latency of right eye was found to be prolonged than left eye in hypothyroidism due to neuroanatomic asymmetries of human striate cortex. According to **Seyal (1981) etal and Kuroiwa (1987)** etal , P100 latency obtained by stimulating the dominant

eye was shorter than the non dominant eye due to neuroanatomic asymmetries of human striate cortex normally.[130]

Analysis of correlations

Our study revealed that there was statistically significant negative correlation exist between serum calcium and TSH in hypothyroidism with 'r' value (-0.22 4) showing significance (0.117) using Pearson's correlation analysis (Table :21) . Findings of our study were supported by the studies of **Rizzoli R (1986) et al[38], Sato K (1987) et al [39] , Shlomo Melmed (2011) et al [40], Gammage MD (1986) et al[121] ,Shivaleela MB (2012) et al [122], Suneel B(2011) et al[123] , Christoph Schwarza (2012) et al[124]** which also revealed negative correlation.

In our study , it was found that there was strong association between the serum ferritin and thyroid hormones (T_3 and T_4) and weak association between serum ferritin and TSH in hypothyroidism with 'r' value (0.083) showing significance (0.568) using Pearson correlation analysis (Table:22) . Our findings were supported by the studies of **Akhter S (2012) et al [51] , Christ-Crain M (2003) et al[117] , Ashuma Sachdeva (2015) et al [108] , Goosen B (1992) et al [118] , Mullner EW (1998)et al [119] ,Tang CK (1992) et al[120]** .

Our study also revealed that there was statistically significant positive correlation between Body mass index (BMI) and TSH in hypothyroidism with 'r' value (0.344) showing significance (0.014) using Pearson correlation analysis (Table:23) The studies of **Knudsen N & Laurberg P (2005) et al[102] , Reineer T (2010) et al[13] , Roel Fsema F (2009) et al[72] , Dall's asta C (2009) et al[73]** were consistent with the findings of our study .

Our study noticed that there was statistically significant positive correlation between lipids (serum total cholesterol ,serum LDL and serum HDL) and TSH in hypothyroidism with 'r' value (0.062) showing significance (0.670) using Pearson correlation analysis (Table:24) . Our study also revealed that there was inverse relationship between serum triglycerides and TSH. Our findings correlated with the studies of **Roopa Murgod (2012) et al[110] , Chan Hee Jung (2003) et al[125] , Lia Scarabottolo (1986) et al[126] , Pearce EN (2012) et al[54] , Mullur R (2014) et al[129]** .

CONCLUSION

SUMMARY AND CONCLUSIONS

- Currently about 4.2 crores of Indians are suffering from thyroid disorders and hypothyroidism being the commonest .
- It is easy to detect and inexpensive to treat , in India about 1/3rd patients with hypothyroidism remain untreated and undiagnosed .
- In our study the majority of them are in overt hypothyroid criteria eventhough they are newly diagnosed , due to lack of awareness of hypothyroid features as it often confuses with other diseases .
- Our study revealed that the impact of hypothyroidism on weight gain , body mass index , lipid profile , serum calcium and ferritin levels which finally lead to Metabolic syndrome.
- As it has females preponderance , this in turn shows its impact in neonates leading to irreversible mental retardation if hypothyroidism left untreated in pregnancy.
- In our study we evaluate electrophysiological parameter like P100 latency of VEP and observed prolongation of P100 latency which suggested central nervous system involvement in hypothyroidism
- As this disorder increases with age, periodic evaluation of hypothyroids using this simple , non invasive electrophysiological test helps to monitor the progression of neuropathy as well as early

detection of asymptomatic polyneuropathy thereby reducing the morbidity.

- Thyroid deficiency also lead to complications like hearing loss, pleural effusion, renal impairment , hyperurecemia, dyslipidemia and insulin resistance, obesity, pericardial effusion and vascular endothelial abnormalities , carpal tunnel syndrome, ascites menorrhagia and iron deficiency anemia .
- Nowadays thyroid test panel has been widely employed for screening and evaluating thyroid dysfunctions .
- So **prevention is better than cure**. **Awareness about hypothyroidism** is utmost important for early diagnosis and to prevent its complications.

FUTURE SCOPE OF THE STUDY

FUTURE SCOPE OF THE STUDY

LIMITATIONS

1. Small sample size
2. Our study doesn't include measurement of serum free thyroxine and triiodothyronine and thyroid antibodies
3. Our study included hypothyroids of tertiary care hospital and not included those attending in other health care sectors .
4. Other types of thyroid disorders were not included.

FUTURE SCOPE

1. Study can be performed in larger number of hypothyroids including all health care sectors .
2. Measurement of serum free thyroxine , triiodothyronine ,thyroid antibodies may add further information about thyroid status .
3. Evaluating other types of thyroid disorders .
4. Follow up study , before and after thyroxine treatment is beneficial.
5. Correlation between overt hypothyroidism and Metabolic syndrome.

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ANNEXURES

CONSENT

FORM

நோயாளிகளுக்கு அறிவிப்பு மற்றும் ஒப்புதல் படிவம்
மருத்துவ ஆய்வில் பங்கேற்பதற்கு

ஆய்வு செய்யப்படும் தலைப்பு :
பங்கு பெறுபவரின் பெயர் :
பங்கு பெறுபவரின் வயது :

		பங்கு பெறுவர் இதனை ✓ குறிக்கவும்
1	நான் மேலே குறிப்பிட்டுள்ள மருத்துவ ஆய்வின் விவரங்கள் நான் படித்து புரிந்து கொண்டேன். என்னுடைய சந்தேகங்களை கேட்கவும், அதற்கான தகுந்த விளக்கங்களை பெறவும் வாய்ப்பளிக்கப்பட்டுள்ளது என அறிந்து கொண்டேன்	☐
2	நான் இவ்வாய்வில் தன்னிச்சையாக தான் பங்கேற்கிறேன். எந்த காரணத்தினாலோ எந்த கட்டத்திலும், எந்த சட்ட சிக்கலுக்கும் உட்படாமல் நான் இவ்வாய்வில் இருந்து விலகி கொள்ளலாம் என்றும் அறிந்து கொண்டேன்.	☐
3	இந்த ஆய்வு சம்பந்தமாகவோ, இதை சார்ந்து மேலும் ஆய்வு மேற்கொள்ளும் போதும் இந்த ஆய்வில் பங்குபெறும் மருத்துவர் என்னுடைய மருத்துவ அறிக்கைகளை பார்ப்பதற்கு என் அனுமதி தேவையில்லை என அறிந்து கொள்கிறேன். நான் ஆய்வில் இருந்து விலகிக் கொண்டாலும் இது பொருந்தும் என அறிகிறேன்.	☐
4	இந்த ஆய்வில் மூலம் கிடைக்கும் தகவலையோ, முடிவையோ பயன்படுத்திக் கொள்ள மறுக்க மாட்டேன்.	☐
5	இந்த ஆய்வில் பங்கு கொள்ள ஒப்புக் கொள்கிறேன். எனக்கு கொடுக்கப்பட்ட அறிவுரைகளின்படி நடந்து கொள்வதுடன், ஆய்வை மேற்கொள்ளும் மருத்துவ அணிக்கு உண்மையுடன் இருப்பேன் என்று உறுதியளிக்கிறேன். என் உடல் நலம் பாதிக்கப்பட்டாலோ, அல்லது எதிர்பாராத, வழக்கத்திற்கு மாறான நோய்குறி தென்பட்டாலோ உடனே இதை மருத்துவ அணியிடம் தெரிவிப்பேன் என உறுதி அளிக்கிறேன்.	☐

பங்கேற்பவரின் கையொப்பம் / ..... இடம்.....தேதி.....
கட்டைவிரல் ரேகை
பங்கேற்பவரின் பெயர் மற்றும் விலாசம்.....
ஆய்வாளரின் கையொப்பம் / ..... இடம் ..... தேதி.....
ஆய்வாளரின் பெயர்.....
மையம் .....
கல்வியறிவு இல்லாதவற்கு (கைரேகை வைத்தவர்களுக்கு) இது அவசியம் தேவை
சாட்சியின் கையொப்பம் / ..... இடம் ..... தேதி .....
பெயர் மற்றும் விலாசம் .....

INFORMED CONSENT FORM

Study Title _____

Study Number _____

Subject's Full Name _____

Date of Birth/Age _____

Address _____

1. I confirm that I have read and understood the information sheet dated _____ for the above study and have had the opportunity to ask questions. **OR** I have been explained the nature of the study by the Investigator and had the opportunity toask questions
2. I understand that my participation in the study is voluntary and that I am free to withdraw at any time, without giving any reason and without my medical care or legal rights being affected.
3. I understand that the sponsor of the clinical trial/project, others working on the Sponsor's behalf, the Ethics Committee and the regulatory authorities will not need my permission to look at my health records both in respect of the current study and any further research that may be conducted in relation to it, even if I withdraw from the trial. However, I understand that my Identity will not be revealed in any information released to third parties or published.
4. I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s)
5. I agree to take part in the above study

Signature (or Thumb impression) of the Subject/Legally Acceptable Representative: _____

Signatory's Name _____ Date _____

Signature of the Investigator _____ Date _____

Study Investigator's Name _____

Signature of the Witness _____ Date _____

Name of the Witness

PROFORMA

PROFORMA

ID NO : **Date :**

NAME : **O.P No :**

AGE / SEX :

ADDRESS :

OCCUPATION :

EDUCATION :

HISTORY

1. **Dietary History : Veg / Non – veg**
2. **Sleep duration : hrs.**
3. **Physical activity : Yes / No**
4. **History of diabetes : Yes / No**
5. **History of hypertension : Yes / No**
6. **Family history of thyroid disorders**
7. **History of steroid or any other drug intake ?**
8. **History of visual disturbances ?**
9. **History any swelling in neck ?**

GENERAL EXAMINATION

Anemia :

Icterus :

Cyanosis :

Pedal edema :

Lymphadenopathy :

CLINICAL EXAMINATION

Temperature : ° F **Pulse : / min**

BP : mmHg **RR : /min**

SYSTEM EXAMINATION

RS **ABDOMEN**

CVS **CNS**

ANTHROPOMETRIC MEASUREMENTS

Height : ……. cm **Weight : ……. Kg**

BMI : ……Kg / m2

BIOCHEMICAL PARAMETERS

Thyroid Profile

T_3 …..ng/ml , T_4 ….µg/dl , TSH ….µIU/ml

Serum Calcium : …..mg/dl

Serum Ferritin : ……mg / dl

LIPID PROFILE

Total cholesterol : …….mg/dl

Triglycerides : ……..mg/dl

LDL : ……..mg/dl

HDL : …….mg/dl

ELECTROPHYSIOLOGICAL TEST

VISUAL EVOKED POTENTIALS

Left Eye : ……msec

Right Eye : …….msec

CONSENT : I hereby give my volunteer consent for the above study.

Signature

MASTER CHART

MASTER CHART (HYPOTHYROIDS)																
S.NO	NAME	AGE&SEX	HT(cm)	WT(Kg)	BMI	T3	T4	TSH	FERRITIN	CALCIUM	T.CHOLESTEROL	TGL	HDL	LDL	VEP(LT)	VEP(RT)
						ng/ml	µg/dl	µIU/ml	µg/l	mg/dl	mg/dl	mg/dl	mg/dl	mg/dl	(P100)	(P100)
1	BALAMMAL	33YRS/F	160	75	29.2	0.8	6.6	43.3	42	11.3	165	85	42	106	98.6	106.8
2	KANI	30YRS/F	162	65	24.8	1.3	11.2	41.6	63.6	7.9	92	90	26	48	100.2	118.9
3	SALINI	39YRS/F	150	60	26.6	1.4	8.6	24.8	22.1	10.6	195	132	38	130.6	97.8	116.2
4	MUTHU KUMAR	44YRS/M	157	70	28.4	1.2	4.8	44.6	41.5	7.9	148	299	22	66.2	101.3	118.4
5	ANANDAN	45YRS/M	165	68	25	1.3	5.2	43.2	42.5	6.6	181	208	38	101.4	120.3	108.5
6	REKHA	25YRS/F	154	72	30.3	1.3	9.4	43.3	41.2	7.3	159	303	46	52.4	100.2	108.7
7	BAGAVATHI	36YRS/F	150	65	28.8	0.3	2.2	47.5	40.5	6.2	224	189	58	128.2	102.3	119.2
8	POOMARI	25YRS/F	157	71	28.8	0.3	3	46.7	36.4	10.3	180	221	56	79.8	99.4	113.4
9	INDHUMARI	23YRS/F	155	59	24.5	0.8	4.9	46.8	87.4	7.8	165	64	45	107.2	98.4	112.3
10	GANESH	39YRS/F	161	65	25	1.8	9.9	14.7	42.1	10.3	166	308	34	70.4	101.6	118.4
11	MANIMEGALA	32YRS/F	158	64	25.7	1.3	4.9	31.4	42.6	6.5	115	78	30	69.4	114.3	98.3
12	SELVAMARI	35YRS/F	145	60	28.5	1.9	4.9	34.6	21	7.3	304	55	67	226	98.3	117.5
13	SASIKALA	35YRS/F	153	68	29	1.9	7.6	27	20	10	164	117	52	88.6	118.2	96.3
14	THEIVANAI	45YRS/F	160	75	29.2	1.7	4.9	42	32	11.1	77	102	18	20.2	95.6	116.9
15	MEGALA	45YRS/F	156	67	27.5	1.9	4.9	44.5	23	7	102	84	40	45.2	100.1	118.5
16	IYYAMMAL	38YRS/F	160	75	29.2	1.4	11	23	38	7.6	168	102	34	113.6	99.4	119.9
17	NESAMANI	48YRS/F	145	60	28.5	0.3	2.8	43.9	42	7.4	234	318	52	118.4	100	121.2
18	SHANMUGAVAL	48YRS/F	153	62	26.4	1.3	5.2	46.8	41	8	225	72	42	168.6	101.1	128.5
19	MARIAMMAL	35YRS/F	154	70	29.5	0.8	4.2	42	62	7.8	151	70	44	93	94.8	117.4
20	MUTHULAXMI	32YRS/F	158	58	23.2	1	5.2	37.2	33	8	142	176	45	61.8	119.8	100.4
21	PETCHIAMMAL	50YRS/F	145	50	23.8	1.6	6.6	33.4	40	6.6	208	148	26	152.4	92.6	131.4
22	DEEPIKA	24YRS/F	154	55	23.2	0.7	3.1	49.3	36	7.2	148	73	45	88.4	99.7	115.8
23	PREMA	36YRS/F	158	65	26.1	1.6	8.5	22.6	39	10.9	133	135	26	80	117.5	98.8
24	PARAMESH	27YRS/F	153	60	25.64	0.9	1.3	31	45	10.9	262	85	77	168	97.2	118.4
25	CHERMAKANI	45YRS/F	164	80	29.8	0.9	6.6	33.1	32	10.8	205	250	42	113	121.6	100.3
26	DEVA	31YRS/F	157	60	24.3	1.2	6	43.2	41	7.9	201	200	43	118	100	118.3

27	KALVATH	35YRS/F	150	70	31.1	0.7	6	48.5	35	7.8	158	70	47	97	98.4	119.3
28	ESSAKI	49YRS/F	156	58	23.86	1.3	4.9	44	23	10.2	270	257	52	166	91.7	118.6
29	PONMALAR	33YRS/F	156	68	27.98	1.6	5.2	44.9	41	9.8	371	223	56	270.4	116.8	98.4
30	PUSHPA	39YRS/F	155	58	24.1	1.6	6.3	43.8	28	9.4	205	137	39	138.6	105.2	123.4
31	JEYA	39YRS/F	154	55	23.2	1.8	7.2	21.9	38	10	158	127	35	97.6	121.5	105.2
32	KAVITHA	30YRS/F	145	58	27.6	1.2	4.9	41.6	26	10.2	200	105	60	119	100	120
33	SARA	28YRS/F	158	60	24	1.2	4.9	41.9	32	9.8	204	103	48	135.4	104.3	119.4
34	SELVAMARI	25YRS/F	151	80	35	1.7	8.6	23.6	41	10	102	90	30	54	101.2	119.2
35	IYAMMAL	32YRS/F	156	74	30.4	1.8	9.1	42.5	39	9.8	181	155	49	101	114.8	92.3
36	MUTHU	32YRS/F	148	54	24.65	1.2	6.6	18.5	39	9.4	286	113	32	231.4	119.6	94.2
37	VANITHA	40YRS/F	160	75	29.2	0.7	5.2	41.8	47	10	267	253	45	171.4	107.2	123.5
38	BENITHA	40YRS/F	156	70	28.8	1.1	8.4	41.1	37	9.9	169	98	32	117.4	119.3	92.6
39	MARISELVI	38YRS/F	149	60	27	0.9	6.6	39.7	40	10	136	80	35	85	110.6	126.3
40	FATHIMUTHU	48YRS/F	156	80	32.9	0.2	2.8	45.7	39	9.5	273	147	40	203.6	128.6	100.1
41	RAMAN	45YRS/M	164	85	31.7	1.8	7.3	44.6	42	10.3	150	60	32	106	108.2	121.3
42	HARI	35YRS/M	160	76	29.6	1.7	9.4	40.5	48	11	106	121	35	46.8	129.3	109.3
43	SARALAN	50YRS/M	170	90	31.1	0.2	2.2	44.3	43	5.21	338	679	110	92.2	108.2	135.6
44	JOHNSON	48YRS/F	168	78	27.65	0.8	4.9	31.3	31	5.76	230	210	37	151	131.2	106.9
45	PARAMAN	50YRS/M	174	90	29.8	0.7	3.1	44.71	100	9.8	168	318	50	54.4	109.1	132.3
46	NAGOOR	49YRS/M	168	85	30.1	1.3	4.9	44	24.8	9.2	122	72	42	65.6	106.8	128.9
47	SANKAR	48YRS/M	145	75	35.7	0.3	2.1	150	35	7	204	103	48	135.4	121.4	105.9
48	VELAVAN	48YRS/M	165	78	28.6	0.1	12.5	53	131.3	7.5	270	157	42	196.6	108.2	121.4
49	RAGUL	30YRS/M	168	88	31.2	1.8	9.1	42.6	9.1	7.4	225	211	38	144.8	118.4	98.6
50	JOSEPHIN	50YRS/M	170	90	31.1	0.7	9.9	2.21	44	7.8	208	200	43	125	99.9	136.3
51	VANNAN	43YRS/M	174	85	28.1	1.16	6.5	16.2	94.6	7.4	102	102	34	47.6	105.8	121.9

MASTER CHART (NORMAL CONTROLS)																
S.NO	NAME	AGE&SEX	HT(cm)	WT (Kg)	BMI	T3	T4	TSH	FERRITIN	CALCIUM	T.CHOLESTEROL	TGL	HDL	LDL	VEP(LT)	VEP(RT)
						ng/ml	µg/dl	µIU/ml	µg/l	mg/dl	mg/dl	mg/dl	mg/dl	mg/dl	P100	P100
1	KANI	25YRS/ F	152	50	21.6	1.7	11.2	0.5	88.4	10	160	180	46	78	95.5	97.8
2	SORIMUTHU	23YRS/	156	54	22.2	1.5	7.3	2.6	90.1	11.2	155	185	45	73	96.8	94.5
3	AMUTHA	29YRS/F	156	50	20.5	0.9	11.2	4.3	80.2	9.6	168	175	35	98	100.1	99.8
4	SELVI	27YRS/F	154	52	21.9	1.2	9.3	3.4	91.1	10.1	156	186	41	78	93.8	98.8
5	PANDIAMM	47YRS/F	160	55	21.48	1.6	9.3	0.3	80.2	9.5	150	180	40	74	100.6	100.1
6	SELVI	25YRS/F	155	53	22.08	2.6	14.5	0.4	100.1	10	160	180	45	78	99.5	100.2
7	MEHABOO	27YRS/F	158	51	20.48	1.9	8.7	0.7	92.2	9.8	165	190	35	92	98.7	100.1
8	RAMANA	27YRS/F	162	55	20.99	1.7	9.3	2.9	88.3	10	120	150	20	70	96.9	98.4
9	SHAHILA	47YRS/F	166	54	19.63	1.8	10.4	0.4	80.2	10.8	154	185	32	85	100.5	99.3
10	KRISHNA	50YRS/F	156	52	21.39	1.7	7.7	0.4	79.2	9.9	140	150	37	73	100	99.3
11	PARVATHI	50YRS/F	161	54	20.8	1.8	8.6	0.6	87.4	9.8	120	150	20	70	99.9	100.1
12	MAYA	27YRS/F	145	45	21.4	1.6	11.2	0.7	89.6	11.1	150	180	38	76	95.6	96.9
13	THANGAM	45YRS/F	148	50	22.8	1.8	11.2	0.3	99.2	9.5	168	175	40	93	100.2	99.3
14	ALEEMA	47YRS/F	140	50	25.5	1.6	10.1	0.6	88.4	10.2	150	180	36	78	100	98.8
15	SANKAR	45YRS/F	152	54	23.3	1.6	10.1	0.5	91.2	9.8	150	175	40	75	100.5	99.3
16	SHANTHI	28YRS/F	161	56	21.6	1.8	10.1	0.3	100.2	9.8	150	180	38	76	95.6	96.9
17	MARI	50YRS/F	147	50	23.1	1.3	10.1	0.5	86.3	9.6	120	150	25	65	99.8	101.2
18	SARASWATH	49YRS/F	164	58	21.6	1.8	5.2	1.5	78.9	10.4	130	160	30	68	100.8	101.1
19	MARIAMMA	40YRS/F	157	60	24.3	1.8	5.2	1.2	82.4	10.1	155	180	29	90	99.8	100.1
20	KAVITHA	25YRS/F	155	56	23.3	1.6	8.7	0.3	94.3	9.8	160	180	44	80	96.9	97.8
21	NISHA	25YRS/F	162	59	22.5	1.8	8.7	0.5	85.6	10	140	150	40	70	100.3	99.6
22	BENASE	23YRS/F	147	50	23.1	1.8	8.7	0.5	82	9.7	145	160	43	70	98.9	98.4
23	THANAM	29YRS/F	156	58	23.8	1.8	8.6	0.6	80.4	10.2	160	180	45	78	98.5	99.2
24	SHANTHI	28YRS/F	160	60	23.4	1.8	11.2	0.3	92.6	9.7	158	185	35	86	100.2	100.3
25	KALA	23YRS/F	148	48	21.9	1.6	11.2	0.7	92.4	10	162	185	45	80	97.6	98.4
26	MUTHU	48YRS/F	154	52	21.9	1.2	11	0.2	94.3	9.9	132	160	40	60	101.8	100.5

27	ANNATHAI	44YRS/F	153	55	23.5	1.6	11.2	0.3	88.3	9.8	158	175	40	83	100	99.6
28	SUNDARI	26YRS/F	161	55	21.2	1.6	11.2	0.3	89.2	9.3	150	175	40	75	95.7	97.8
29	JEBAKANI	49YRS/F	154	56	23.6	1.8	5	0.9	74	10.1	158	185	35	86	99.6	100
30	VANITHA	28YRS/F	149	50	22.5	1.8	4.9	1.1	72.3	10	156	180	30	90	96.9	98.7
31	PREMA	46YRS/F	154	55	23.2	1.6	5	2.5	67.2	9.9	155	170	36	85	101.2	100.5
32	BRISKILA	50YRS/F	162	61	23.2	1.9	5.2	1.3	72.1	9.8	151	180	40	75	101.5	100.3
33	RAJES	44YRS/F	159	57	22.6	1.8	9.2	0.5	88.3	9.9	162	180	40	86	99.3	100.5
34	MEENA	49YRS/F	152	58	25.1	1.4	11.3	0.5	92.2	10.1	160	175	45	80	100.4	99.3
35	SEETHA	27YRS/F	148	50	22.8	1.3	10.1	2.8	86.2	11.1	156	175	41	80	95.7	96.5
36	BEEVI	50YRS/F	163	60	22.6	1.2	9.7	1.9	77.3	9.9	120	150	30	60	99.8	101.6
37	BUVANESH	44YRS/F	164	62	23.1	1.4	5.2	1.9	80.2	9.8	131	160	39	60	98.7	100.2
38	NESAMANI	48YRS/F	161	63	26.6	1.3	11	1.4	88.6	9.7	146	155	40	75	100.5	99.4
39	SHANTHI	48YRS/F	157	60	24.3	1.4	10.2	0.5	74.8	9.6	144	160	42	70	99.6	100.9
40	SUNDARI	48YRS/F	155	54	22.5	1.8	11	0.2	92.1	10	150	175	40	75	100.1	99.5
41	MUTHU	35YRS/M	170	65	22.4	1.7	11	0.9	90.3	10.4	160	180	44	80	100.3	99.2
42	DEVAN	38YRS/M	174	70	23.1	1.4	11	0.8	84.8	9.4	164	180	38	90	99.7	100.1
43	SURESH	40YRS/M	152	55	23.8	1.3	5.2	0.9	79.3	10	150	165	37	80	100	99.5
44	Ganesh	35YRS/M	148	48	21.9	1.8	8.6	0.6	83.2	9.8	155	175	38	82	98.7	99.4
45	Moorthy	35YRS/M	165	64	23.5	1.7	8.4	0.6	86.1	9.7	143	165	41	79	97.6	98.4
46	Velavan	39YRS/M	171	65	22.2	1.4	11.1	1.1	91.2	10	123	150	30	63	98.8	99.4
47	Nainar	45YRS/M	174	72	23.8	1.3	9.3	1.6	86.4	10.6	150	175	40	75	100.8	99.1
48	Krishnan	49YRS/M	168	65	23	1.9	10.7	0.6	90.6	9.8	162	175	43	84	99.6	101.2
49	Ravi	47YRS/M	172	66	22.3	0.9	11.2	4.3	82.6	10.3	150	175	40	75	98.9	100.1
50	Madavan	50YRS/M	174	75	24.8	1.3	5.2	0.9	74.2	10	145	155	39	75	101.1	99.8